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Outlook on Tuberculosis.—Thirty years ago there were not more than two or three sanatoria in Great Britain and only one dispensary. To-day, in England and Scotland, there exist 300 sanatoria and hospitals and 500 dispensaries. This means that machinery is in operation for the detection of tuberculosis at an early stage, for the improvement of environmental conditions in the widest sense, for the treatment of the various forms of tuberculosis with a view to cure, and for the segregation and hospitalization of more advanced cases. When one considers the general apathy in evidence fifty years ago on the whole subject of tuberculosis, one is impressed by the extraordinary change in outlook which has occurred. In Scotland, the death-rate from all forms of tuberculosis has fallen from 336 per 100,000 in 1879 to 97 in 1928, and the death-rate from pulmonary tuberculosis from 231 per 100,000 to 68. A comparison of the epidemiological records of different countries points to the conclusion that the tuberculosis index of a given area is dependent on and is governed by the degree of intelligent action on the part of health authorities and of coöperation on the part of the inhabitants. The tuberculosis scheme needs to recognize these cardinal facts: (1) that infection is widespread throughout a community; (2) that it is contracted for the most part in childhood; and (3) that, once established, it continues to exert its influence throughout the life of the individual, either securing protection (immunity) from the consequences of further exposure, as happily occurs in the majority of individuals, or by producing recurrent disturbances which are precipitated by many different causes (personal and environmental) and which vary endlessly in kind and in degree; and (4) that in proportion as the resistance of the infected individual is kept high, these disturbances are likely to be few and relatively slight, and, in proportion as the resistance is lowered by any cause, the infection is apt to spread, and existing lesions tend to be activated and extended.—*The Outlook on Tuberculosis: Changing Orientation, Robert Philip, Brit. M. J., January, 10, 1931, no. 3653, 43.—(M. E. P.)*

Tuberculosis and Preventive Medicine.—President Eliot of Harvard once remarked that the physician of the future would be largely engaged in preventive medicine. If one considers the ever-broadening scope of official health departments, together with the extensive activities of voluntary health associations, the trend is readily recognizable. Among the latter organizations is the great Rockefeller Foundation, which, since its founding in 1913 has spent upward of $144,000,000, and in 1928 alone over $21,000,000 for the development of medical

science and prevention of disease throughout the world. Through its efforts yellow fever, malaria and hookworm disease have been greatly reduced or almost banished. Another notable voluntary health agency is the National Tuberculosis Association, founded twenty-five years ago, which derives an annual income of nearly $300,000, mostly from a 5 per cent tax upon the receipts of the Christmas Seal Sale throughout the United States, and one of whose noteworthy undertakings is research work carried on by able and recognized scientists. Valuable work in preventive medicine is also being carried on by some of the great life-insurance companies, notably the Metropolitan of New York, which in the last fifteen years has expended a total of $18,709,000 in its public-health campaign for industrial policy-holders and others. It appropriated $200,000 for the Framingham Demonstration, and during the years of its existence the tuberculosis mortality in Framingham declined from 121 per 100,000 per year from 1907–1917 to 38 per 100,000 in 1923. In its health advertising and literature this company furnishes an excellent example of how to "sell" health, which, as Rosenau says, is the greatest problem, that is, to bring preventive medicine to the people. The mortality statistics for the past two decades show a tremendous reduction for such diseases as diphtheria and typhoid fever, and a marked fall for tuberculosis and diseases of early infancy. On the other hand, mortality from heart disease and cancer has increased. The average life expectancy in 1926 was 57.7 years, compared to 33 years a century ago, while prior to the discovery of America it was 18 years. The age-periods at which the maximum mortality from different diseases occurs is interesting: for pneumonia, the high points are under 5 and over 65, for tuberculosis under 5 and from 20 to 35, the last the most economically valuable period of life. *Tuberculosis:* In the registration area of the United States the tuberculosis mortality under one year in 1926 was 64.6 per 100,000 and under five 39.6; between five and nine years it was only 11.9. The infection in the case of these very young children must come from near at hand and the means of avoidance is to remove infants from an infected environment, according to Grancher's placement plan. A second and newer method is to treat uninfected but exposed infants with the so called *BCG* vaccine. Many statistics, mostly French, show a striking diminution of mortality from tuberculosis among vaccinated infants in infected families. Calmette and Plotz have recently published their results among 2,368 vaccinated infants and 4,854 unvaccinated controls, and further state that *BCG* has been given to 132,000 infants from July, 1924, to January, 1929, without a single case of deleterious effects; also, that the infant mortality in France has been reduced to one-sixth of the ordinary expected figure. Calmette finds reason to believe that protection persists over four years. Otis adds that this vaccine could well be administered to older children and adults particularly exposed to infection, after preliminary tuberculin testing. Calmette has employed the oral method of administration chiefly, the child being removed from the source of infection for a period of four weeks while immunity develops. The Pasteur Institute of Paris will furnish the original strain to public-health authorities if requested and in the United States W. H. Park, of the New York City Health Department, is carrying on studies with it. In the United States after the age of 14 the tuberculosis mortality curve rises and from 15 to 19 is 78.7 per 100,000, and from 25 to 34 is 120.4, higher than that of all other capital diseases together. In explanation, it is suggested that at this period young men and women are entering the strenuous activities of life and careers under exacting and competitive conditions. The routine of eight hours a day begins often under unhygienic indoor conditions. Sufficient nourishing food is often neglected and the importance of recuperative rest not appreciated. After work, diversion is sought in amusements which may tax mind and body, and sufficient sleep is neglected. Chronic fatigue comes on insidiously and finally a real breakdown from tuberculosis. The remedy is plain: to modify or change one's mode of life so far as possible under present civilization and competition. On returning home from work, a half hour's rest in the recumbent position, especially for young women, is a valuable relief. The evening, as a rule, should be spent quietly and the sleeping room be well ventilated. Occasional diversion is natural but should not be overexciting. Also, some physical exercise is necessary, preferably outdoors, but should not be taken when one is thoroughly tired out. A longer vacation is advocated for young women in industrial or commercial life. *Pneumonoconiosis or Silicosis:* The granite-cutting industry in New England is important. A most prevalent disease among the workers is pneumonoconiosis, often finally resulting in chronic pulmonary tuberculosis. McFarland (*Journal of Industrial Hygiene*, August, 1927) reports the tuberculosis death-rate among granite-cutters as 1095.5 per 100,000, or about 11.5 times the average. In 1922 Hoffman, in Vermont, found a similar state of affairs. If the granite-worker leaves his occupation the silica

deposits in his lungs may disappear, but at the end of seven years (Pitchford, *Journal of Industrial Hygiene*, 1927, ix, 109) a little over half the cases have developed tuberculosis. Preventive measures which are applicable are periodic examination, shorter hours, avoidance of dry drilling, use of masks and compressed-air apparatus to remove dust, and removal from the industry of workers having appreciable deposits in the lungs.—*The Prevention of Disease: Some Applications of Preventive Medicine, Prize Essay, New Hampshire Med. Soc., E. O. Otis, New England J. M., December 4, 1930, cciii, 1143.*—(*A. P.*).

Tuberculosis and Public Health.—The progress and efficiency of current preventive measures and the behavior of the death-rate in tuberculosis are two important subjects. Antituberculosis campaigns, in addition to creating machinery for the control of tuberculosis, have assisted and stimulated general public-health measures for the common welfare and have helped to direct the broad policy of preventive medicine along its present channels. Higher standards of housing and of environmental hygiene, promotion of social legislation, personal and domestic hygiene, and prevention of disease have been furthered by the antituberculosis campaigns. The dispensary is an educational centre and "clearing house," related to the homes of the people and to the institution for treatment. It performs every possible social, medical and preventive service. It becomes a centre for the diagnosis and treatment of a variety of chronic diseases of the lungs. Institutional provisions take the form of the sanatorium and hospital. Suitable care and treatment for tuberculous individuals, prevention of possible massive infection of contacts, and improvement of environment are some of its problems. Statistics in Glasgow show that tuberculosis is rapidly declining as a chronic affection of the middle-aged, but remains unaffected as an acute affection of young adults.—*Tuberculosis and Public Health, A. S. M. MacGregor, Brit. M. J., November 1, 1930, no. 3643, 724.*—(*M. E. P.*)

Tuberculous Patients and Change of Physicians.—It has been widely accepted as a fact that the tuberculous person flits from physician to physician, does not wish to know what ails him, and is inclined to be dissatisfied with any treatment given. But according to the history of 1499 patients obtained by the National Tuberculosis Association in a study of experiences prior to sanatorium admission, the patient who so conducts himself is unusual. The history of the sanatorium patient indicates that in his moves with respect to the medical profession he ordinarily exhibits merely a quite legitimate interest in his own welfare. Approximately 47 per cent of 1480 patients reporting on the question had consulted only one physician before finding out that they were tuberculous. After learning that they had tuberculosis, 63 per cent accepted this diagnosis without further consultation. The number of changes in physicians averaged 0.86 per man and 0.67 per woman prior to ascertaining the diagnosis and 0.57 and 0.48 afterwards. A change of location was responsible for 13.5 per cent of changes before and 13.2 per cent of changes after the patient found he was tuberculous. The attending physician was directly responsible for 19.2 per cent of the changes before and 27.5 per cent of the changes after the diagnosis was made, apparently activated almost exclusively either by the feeling that another could make a more authoritative diagnosis or was better fitted to advise the necessary treatment. Closely allied to changes due to direct reference are those to a clinic through which one sanatorium required applications to be filed. Considerably more changes were made for the purpose of establishing the diagnosis before the patient learned that he was tuberculous than afterward. Patients reported being displeased at receiving no diagnosis or being told nothing was the matter or because of dissatisfaction with the diagnosis given. After being apprised that they were tuberculous they sometimes turned to another physician for verification or an X-ray picture or because of a change of diagnosis. Because of treatment considered unsatisfactory, 189 changes were made prior to learning the diagnosis, 62 subsequently. In 70 instances prior to diagnosis, and 5 after, there was dissatisfaction with both diagnosis and treatment. The data indicate that patients are generally much less disturbed when they learn they have tuberculosis than when in doubt and that without a definite diagnosis of which they are convinced they will seek another physician.—*The Number of Physicians Consulted by Tuberculous Patients and the Reasons for Changing from One to Another, L. R. Williams and A. M. Hill, New England J. M., October 16, 1930, cciii, 782.*—(*A. P.*).

Training of General Practitioner in Tuberculosis.—The time has arrived when the mortality rate in tuberculosis will remain stationary unless the practising physician be taken into consideration and be trained, particularly in early diagnosis. The present condition can be met, in part at least, by instruction of medical students and by

postgraduate instruction. Inadequate training has come about through lack of clinical material in the teaching hospitals and absence of teachers interested in the subject. In many countries tuberculosis patients are not admitted to general hospitals. Besides this, most of such patients are seen by public-health officers rather than by practitioners, and such patients are cared for by insurance physicians. Sir Robert Philip has pointed the way in Great Britain by having students transported to tuberculosis sanatoria for a part of their training. The physician of the coming years will be more and more interested in prevention and must thus appreciate the signs and symptoms of early departtures from health. Training in tuberculosis will help develop this point of view. At present the general practitioner sees no particular reason why he should interest himself especially in tuberculosis. Would it be better to allow him to do part-time health work and thus to come in contact more with this disease? One difficulty in the way of the general man attending postgraduate courses is an economic one.—*The Training of General Practitioners in Tuberculosis, S. V. Pearson, J. State Med., July, 1930, xxxviii, 383.*—(*H. S. W.*)

Teaching of Tuberculosis.—A plea is made to present the study of tuberculosis to students in such a way that able medical graduates will enlist in the race for the search of the cure or prevention of tuberculosis.—*On the Teaching of Tuberculosis, S. J. Maher, Brit. M. J., October 11, 1930, no. 3640, 605.*—(*M. E. P.*)

Tuberculosis in Jamaica.—Tuberculosis among the colored natives in the West Indies is a very fatal disease, some of the epidemiological features of which have been studied in Jamaica. The ordinary type of chronic pulmonary tuberculosis, while frequently encountered, is by no means the prevalent type there as it is in Europe and the United States. The majority of Jamaicans who die of tuberculosis have a rapidly progressing type of the disease. Data are unreliable, but they show, for the last ten years, a fluctuation of from 200 to 133 per 100,000. However, this leaves out of the picture many cases diagnosed "fever," "asthma," etc., which double or treble the number reported as tuberculosis. In general, the trend of reported cases is lower, but for 1927 the reported rate for Kingston was three times that of the United States. The highest incidence is in early adult life (before age 20). "Poorhouses," which are the only provision for indigent cases, shelter many patients; the average length of residence of those who died in one of these was 26 days and of those who survived was 116 days. (In one such house, 111 died in one year and 23 were discharged.) A tuberculosis dispensary, organized in 1928, examines, diagnoses and treats patients and has an eye to statistical data. In the first six months of the dispensary, 527 patients were examined; 236 of these had no tuberculosis and 77 were suspects; nearly all the remainder had the disease. Of 169 of the tuberculous patients seen in the dispensary, 91 (53.8 per cent) were dead at the end of the first year of the dispensary's existence; in other words, this number had died within 6 to 12 months of diagnosis. Forty-two per cent of the dead had an illness of not over eight months' duration. Of another group, the average duration of the disease was 14 months, and of a still smaller group the average age duration was about two years. Living quarters of the poor are most wretched, unsanitary and crowded, and are so arranged as to facilitate both domiciliary and promiscuous contacts between the ill and the healthy. The disease often all but decimates almost the entire family within a comparatively short time. Frequent instances are seen of direct transmission of the disease from one member of the family to another. The hot, dry climate is unfavorable to the life of the tubercle bacillus, but the dark crowded huts offset this advantage. Remedial measures of an educational sort will be worthless in many instances because of gross ignorance. In such circumstances segregation of the sick promptly upon detection should be done, which means that hospitals for the care of such cases are needed and are needed much more than are sanatoria at present, although obviously these should follow. A general educational barrage should be laid down. Diminution of overcrowding and improvement in housing conditions are sadly needed. The detection of early tuberculosis in Jamaica must await the satisfactory meeting of the issues that present themselves at present. In many instances young, healthy men leave their rural homes for the crowded towns, develop tuberculosis and return home to spread it still further. Such migration should be prevented when possible. A public-health service should investigate homes where disease is found and should do "case hunting." Improved methods of registration and of collecting vital statistics are needed.—*Tuberculosis in Jamaica, E. L. Opie and E. J. Isaacs, Am. J. Hyg., July,* 1930, *xii, 1.*—(*H. S. W.*)

Antituberculosis Work in Italy.—Italy has a population of approximately 40,000,000 and last year had 60,000 deaths from tuberculosis, that is, about 150 per

100,000 inhabitants. The death-rate is very much higher in the northern than the southern part of the country. It is higher among women. The morbidity is gradually becoming reduced among adults, but has not changed in infants. The National Federation against Tuberculosis and various societies have combined in a very successful antituberculosis campaign. Each citizen now has to be insured against tuberculosis. There are 200 dispensaries throughout the country where diagnostic, therapeutic and prophylactic work is carried on. These have facilities for pneumothorax treatment and radiation therapy. Tuberculin is but little used. There are 23,000 beds in 302 institutions.—*Einiges über die Tuberkulosefürsorge in Italien, R. Ferrari, Deutsche med. Wchnschr., June 13, 1930, lvi, 1011.—(H. S. W.)*

Tuberculosis Control in Holland.—The author reviews the system of tuberculosis control carried out in Holland, which is accordingly divided into sanatorium and dispensary districts. During the past 8 years the mortality dropped from 13 to 8.42 per 10,000 inhabitants. The number of associations for tuberculosis combat and health increased from 424 in 1921 to 711. The number of first applications to dispensaries increased from 16,572 in 1924 to 26,250 in 1928 and in about half of the applicants tuberculosis was found. The number of open cases of tuberculosis during the four years varied between 20.7 to 23.6 per cent, being fairly constant, while the number of children up to 14 years with a positive Pirquet was about 45 per cent. There are available 3,117 sanatorium beds and several hundred hospital beds.—*Acht Jahre Tuberkulosebekämpfung in Holland, R. N. M. Eykel, Zeitschr. f. Tuberk., 1930, lv, 389.—(H. J. C.)*

Seasonal Variations in Pulmonary Tuberculosis.—Between the years 1923 and 1928, 98 patients in Stephani's sanatorium at Montana, Switzerland, were studied clinically (auscultation, spirometry, arterial pressure and weight) and roentgenographically, and also had numerous observations of their cutireaction, sputum, sedimentation, urine, and Arneth's leucocyte formula. Of these, 84 showed a typical and undeniable deviation to the left during the first trimester of the year. In 9 cases followed for a number of years this was repeated each year. There was also an autumnal deviation in 38 of 59 cases studied but less marked and briefer in duration. The conclusions to be drawn seem to be that autumn and spring, especially the latter, are dangerous periods for those with pulmonary tuberculosis. Sanatorium physicians should counsel caution against making abrupt changes in climate in early spring, at a time when general resistance is on the wane.—*Le fléchissement printanier de la résistance générale chez les tuberculeux pulmonaires, J. Stephani and G. Troaurd-Riolle, Rev. d. l. Tuberc., December, 1929, x, 857.—(A. P.)*

Tuberculosis in Old Age.—Tuberculosis in old people is by no means rare. In fact, it is frequent to find recent or recently reactivated processes in lymph nodes, lung or other organs. Arnstein found that 27 per cent of all old people who had died of other diseases than tuberculosis had active tuberculous foci. Anders found recent lymph-node lesions in 35 per cent of all old people. The tuberculous lesions in old age show two definite characteristics: they originate frequently by haematogenous spread and they show a definite tendency to fibrosis. The various forms of disseminated tuberculosis which are frequently observed in childhood are found again not infrequently in old age. The reason for the occurrence is probably the fact that the tuberculin allergy is usually high in senescence, and on the average considerably higher than in the middle period of life. In this regard old age behaves similarly to childhood. The diagnosis of pulmonary tuberculosis in senescence is very difficult. The physical signs are frequently obscured by chronic bronchitis and emphysema. The diagnosis of activity should be based chiefly on the symptomatology. Extrapulmonary lesions too are frequently so atypical as to present great diagnostic difficulties. In the treatment of tuberculosis in senescence, rest and the avoidance of stimulation are the chief factors. Pneumothorax may be used in a few selected cases in which the circulatory system is in good shape and in which emphysema is not marked. Since high allergy seems to be a common feature in tuberculosis in senescence attempts to reduce this allergy by careful tuberculin treatment appear hopeful. Especially in extrapulmonary lesions have good results been obtained by this treatment.—*Bemerkungen zur Alterstuberkulose, insbesondere deren Therapie, A. Müller-Deham, Wien. klin. Wchnschr., December 4, 1930, xliii, 1510.—(M. P.)*

Congenital Tuberculosis.—The existence of congenital tuberculosis is established beyond doubt. Even before the tubercle bacillus had been discovered cases were reported in which stillborn infants of tuberculous mothers showed far-advanced tuberculous lesions. The infection is probably never a true germinal infection, but is transmitted by the placenta. Placental lesions have been

demonstrated by Schmorl and his school, while tubercle bacilli have been found in the placenta, in the blood of the umbilical cord, and in tissues of stillborn infants. Most congenital infections occur probably during birth, when a traumatic communication between maternal and foetal circulation may be established. But Baumgarten's theory that this placental infection accounts for the majority of cases of tuberculous disease has been discarded. The infection may be transmitted by the amniotic fluid if a tuberculous focus is present in the placenta or in the membranes. Up to the present time there are only about 40 well authenticated cases of congenital tuberculosis on record. The first foci of disease are most frequently found in the liver and the periportal lymph nodes. Bacilli may be carried through the inferior vena cava into the right ventricle, from there through the open foramen ovale and the ductus Botalli into the systemic circulation, and foci may be produced in any part of the body, or miliary tuberculosis may occur. The lung is usually not prominently infected because of its meagre blood supply during foetal life. Infected amniotic fluid may produce intestinal infection, or, by aspiration, respiratory infection, or primary middle-ear infection may occur. With all these different possibilities of infection the clinical results are very different. The diagnosis of congenital tuberculosis must consider the following points: An active tuberculosis of the mother must be demonstrated. Tuberculin allergy should be demonstrable in the child in the 3rd or 4th week after birth. In premature infants the tuberculin allergy may occur later or not at all. The clinical symptoms point usually to an infection of the intraäbdominal organs and they are always present within the first few weeks of life. The postmortem findings are of dominant importance. A primary complex in the liver and the periportal lymph nodes is convincing proof of congenital infection. Lesions which are so far advanced that they could not have developed during the life of the infant constitute sufficient proof. The child should have been isolated from its mother immediately after birth in order to exclude the possibility of a postnatal infection. The prognosis of congenital tuberculosis is practically hopeless. The treatment should be the same as that of infantile tuberculosis.—*Die angeborene Tuberkulose, M. Zarfl, Wien. klin. Wchnschr., October 2, 1930, xliii, 1231.*—(*M. P.*)

Congenital Tuberculosis.—*Case Report:* A male, full-term child, was born with a weight of 2,600 gm. His mother, 17 years old, had a caseous pneumonia of which she died eleven days after delivery. The mother's disease was first wrongly diagnosed as puerperal fever, and the child was not isolated until seven days after birth, when the proper diagnosis was made. His weight increased normally up to the seventh week. On the thirty-fifth day he reacted positively to 0.1 mgm. tuberculin intracutaneously; before this, all tuberculin tests had been negative. His temperature was normal up to the middle of the fourth week. In the third week a roentgenogram showed a pneumonic infiltration in the left lung, without clinical findings and without symptoms suggesting this lesion. Three weeks later the clinical findings were characteristic of a pneumonia and they remained unaltered until death which occurred on the fifty-first day. Marked general symptoms, such as gastrointestinal disturbances and rapid loss of weight, started only in the seventh week. The necropsic findings showed caseated lymph nodes at the hepatic hilum, numerous conglomerate tubercles in the liver and in the spleen. Similar foci were numerous in the lungs. In the left upper lobe a larger subpleural focus was found. The tracheobronchial lymph nodes on the left side were caseated but much smaller than those at the hilum of the liver. The retroperitoneal lymph nodes were caseated, and the kidneys showed numerous small tubercles. The brain was free. These findings are interpreted as being caused by an intrauterine haematogenous infection. The pulmonary findings are probably due to a secondary inhalation infection. Both the clinical picture and the late appearance of tuberculin allergy make it likely that the infection occurred during or shortly before delivery.—*Ein Fall von kogenitaler Tuberkulose, S. Feilendorf, Klin. Wchnschr., October 11, 1930, ix, 1921.*—(*M. P.*)

Tuberculosis in Infants.—This paper is a report of all cases of tuberculosis in infants admitted to the *Kaiser Franz Josefs Spital* in the years 1926 to 1930. The total number was 180. In judging the time of the probable infection, the general rule was adopted to assume that the infection occurred not later than six weeks preceding the first positive Pirquet reaction. When definite clinical symptoms or roentgenologically demonstrable pulmonary lesions were present it was assumed that infection must have occurred at least eight weeks before such findings were recorded. On this basis, 18 per cent of all infections occurred in the first three months, 27 per cent in the second three months, and 55 per cent in the second half-year. In 77 per cent of the cases it was possible to find the source of infection. The majority of them occurred in the family,

but it must be assumed that, in most cases in which a source of infection could not be established, infection was probably due to a contact outside the family. It was not possible to establish a definite relation between the severity of the disease and the type of the source of infection. The statement of Eliasberg that acute miliary tuberculosis, tuberculous meningitis and caseous pneumonia occur chiefly in infants from families free from tuberculosis could not be confirmed. The mortality of infants whose source of infection was unknown was 30 per cent; of those infants whose source of infection was known, it was 70 per cent. The prognosis depends in some measure on the time of infection. Infants who were infected during the first three months had a mortality of 61 per cent, those whose infection occurred in the second three months had a mortality of 42 per cent, and infants infected during the second half year had a mortality of 37 per cent. Infants who survived a severe infection seemed to be well protected against later disease, while infants who had only a slight tuberculosis of the hilar lymph nodes without marked clinical symptoms showed a larger percentage of subsequent meningitis. The general course of the disease was strikingly benign in many cases. It is particularly noteworthy that infants with severe pulmonary lesions frequently recovered well. The temperature was very variable, especially since tuberculous infants are prone to develop a multiplicity of complications. Many sudden rises in temperature could not be explained by any change in the clinical or roentgenological findings. The nourishment of tuberculous infants is an extremely difficult problem. These infants usually have a poor appetite and it is frequently necessary to vary the nourishment considerably. Vomiting is frequently observed and no medicinal treatment appears to give any relief. It usually disappears with the general improvement of the child. The tuberculin allergy can usually be demonstrated by the simple Pirquet test. This was positive in all cases with very few exceptions, including agonal cases of miliary tuberculosis and meningitis. Two cases were observed which did not react to the Pirquet test nor to the intracutaneous injection of 1 mgm. of tuberculin; in these cases the diagnosis was made on the postmortem table. The most frequent intercurrent diseases were acute rhinopharyngitis and purulent otitis media. Tuberculous lymphadenitis of the neck exerted a very unfavorable influence on the clinical course. Nonspecific pneumonia occurred in several instances without ill effects. The following acute infectious diseases occurred: laryngeal diphtheria 5 times, 4 of which died; nasal diphtheria 4 times; chickenpox 17 times; whooping-cough 7 times; measles 12 times. Diphtheria and chickenpox do not seem to be more dangerous for tuberculous infants than for nontuberculous ones. The same is probably true for whooping-cough. The well known danger of measles is not only due to the reactivation of tuberculous foci but to the pneumonia following measles. As soon as measles was diagnosed in any infant the rest of the infants received convalescent serum. Out of 10 cases treated with convalescent serum 2 developed measles in a light form, but one developed pneumonia and died. The treatment consisted chiefly of general hygienic care in which the necessity for open-air treatment is emphasized. General heliotherapy when necessary with artificial light sources was practised. In extrapulmonary lesions local heliotherapy was used. The most important part of the treatment is proper nourishment. Pneumothorax was not used. Unilateral pulmonary processes are rare in infants and most of them are epituberculous lesions which are well resorbed without pneumothorax treatment. In a small group of infants a rather latent disease was observed, manifested only by positive tuberculin reaction, slight enlargement of the hilar shadows and slight general symptoms. This type of disease usually heals well but some infants of this group develop meningitis later. Epituberculous processes have a good tendency to heal. They are always characterized by massive roentgenological signs and by a practical absence of clinical signs. The infiltration in most cases occurs around the primary focus. The author believes that these infiltrations are due to toxins of the tubercle bacillus and that they do not represent a true tuberculous process. Typical scrofulosis was rare, but keratitis and conjunctivitis, spina ventosa and cervical adenitis were relatively frequent and showed a good tendency to heal. Destructive pulmonary processes offer an almost hopeless prognosis; most of these infants die of miliary tuberculosis or meningitis. Only one case of congenital tuberculosis was observed, and only one case of primary intestinal tuberculosis. Of the 180 cases 51.1 per cent were discharged as improved, and 44.4 per cent died. Latent infection occurred in 33 cases, tuberculosis of the hilar lymph nodes in 21, epituberculosis in 27, pulmonary tuberculosis in 54, miliary tuberculosis (exclusive of terminal developments) in 21, peripheral tuberculosis in 36, tuberculous meningitis in 6 cases. The causes of death were as follows: Miliary tuberculosis in 27, destructive pulmonary tuberculosis in 36, tuberculous meningitis without miliary tuberculosis in 6, intercurrent diseases in 11. A plea is

made for much more careful prophylaxis. It is postulated that all pregnant women should be examined for tuberculosis and that no infant should be permitted to live in coresidence with a tuberculous patient. The paper is concluded with brief case reports of 20 of the more interesting cases.—*Ueber Säuglingstuberkulose, S. Feilendorf, Wien. klin. Wchnschr., October 23, 1930, October 30, 1930, November 6, 1930, xliii, 1311, 1343, 1369.*—(*M.P.*)

Pneumonic Phthisis of Measles in Infancy.—It has long been recognized that the pulmonary infections complicating measles can produce bronchial dilatation, and can also bring about a clinical picture precisely like that of pulmonary tuberculosis. The presence of a positive Pirquet reaction has led many physicians erroneously to consider a very large number of the pulmonary complications of measles as tuberculous in origin. The pediatric axiom that measles may "light up" a case of tuberculosis has led to many a false conclusion which may be set right only if the patient comes to autopsy. The clinical conception of "pneumonic phthisis of measles" persists. The condition entails much hard work and observation in order to establish an accurate diagnosis. There is some relation between measles and whooping-cough from clinical and epidemiological points of view. An attack of measles may cause an apparent recurrence of pertussis dating back one or two years. And the commonest complication of measles in infancy is the so called "whooping-cough-pneumonia," which often runs a very slow course, so similar to that of tuberculous pneumonia as readily to be confused with it. Thus, in view of the inadequacy of our clinical methods of investigation, we must rely on biological tests and on direct bacteriological examination of secretions and excretions, to establish the tuberculous nature of such conditions.—*De la phtisie pneumonique morbilleuse chez les enfants, W. Mikulowski, Arch. d. Méd. d. Enf., December, 1930, xxxiii, 711.*—(*P.J.W.*)

Subacute Miliary Tuberculosis in Infants.—A white female infant, three months of age, had a rise of temperature to 100.2°F., being otherwise free from symptoms. When next seen at the age of five months it was found that the father was receiving treatment for active pulmonary tuberculosis. A Pirquet test on the infant at that time was positive. X-ray revealed "extensive miliary infiltration of both lungs, probably miliary tuberculosis." This was verified by a second picture. Clinical examination was negative. One week later, the child presented a red, painless, extensive swelling of the right ankle, without any roentgenographic changes. Two months later, when the infant was 7 months old, X-ray revealed that the miliary lesions in the left lung had disappeared, though remaining in the right. A second Pirquet test three weeks later was strongly positive. The temperature throughout ranged from 100° to 100.5°F. The patient died at the age of 8½ months. Necropsy was not obtained. The spleen was not palpable at any time. There was a poor gain in weight, but no actual loss. The mild course of the disease, together with the clearing of the process in the left lung, made it evident that the patient suffered from the subacute rather than the acute form of miliary tuberculosis.—*Subacute Miliary Tuberculosis, Fatal Case in an Infant, with Roentgenologic Evidence of Healing, J.S. Uhr, Am. J. Dis. Child., December, 1930, xl, 1269*—(*P.J.W.*)

Classification of Childhood Tuberculosis.—The classification of childhood tuberculosis according to chronological stages in the development, as advocated by Hamburger, differentiates an incubation period, an early stage with the primary complex and the secondary stage, and a late or tertiary stage. The biological incubation period, that is, that period from actual infection to the appearance of tuberculin allergy, is probably fairly constant. The actual measurement of this period depends on the amount of tuberculin which is used for testing. Since it is not always possible to draw a sharp line between the primary and secondary stages, Hamburger advocated differentiating only an early and a late stage. The early stage would then comprise the development of the primary complex and all so called secondary manifestations. The earliest secondary manifestations which are usually observed within the first three months after infection are phlyctenulae, erythema nodosum, exudative pleuritis and tuberculous meningitis. Tuberculin allergy is very high during this period. Other early manifestations are coxitis, gonitis, spondylitis and spina ventosa. Various tuberculides are frequently observed during this period. The pulmonary lesions of the early stage are characterized by perifocal inflammation and haematogenous propagation. At puberty the reaction of the body is markedly changed. Multiple foci in various organs are much less frequent and the most frequent lesions are limited to one organ system, most frequently to the lung, less often to the kidneys, to the iris or, as lupus vulgaris, to the skin. While Hamburger's classification is based entirely on clinical data, Ranke's classification is based on morphological characteristics.—*Die Stadienein-*

teilung der Kindertuberkulose, R. Wagner, Wien. klin. Wchnschr., November 6, 1930, xliii, 1382.—(M. P.)

Tuberculous Infection of School Children.—Studies of tuberculous lesions in childhood have shown that the transition from latent to clinically manifest disease is often defined with much difficulty and that some latent lesions are more extensive than those that are accompanied by symptoms and physical signs. These studies have also demonstrated that a considerable number of children who suffer with clinically manifest tuberculosis escape the attention of parents, teachers, school nurses and physicians, even though medical inspection is as effective as possible. Minor tuberculous lesions of the lung are not recorded on roentgenograms because small foci of consolidated lung tissue, even when they have undergone caseation, are not sufficiently opaque to X-rays. When calcium is deposited in caseous tissue very small lesions become conspicuous, even though the amount of calcium present is not enough to change materially the consistency of the caseous material. Tuberculous lesions may resolve completely or in part, but dissolution of lesions is retarded, if not wholly prevented, by caseation. Tuberculous foci that have undergone calcification persist throughout life as scars readily recognized in roentgenograms unless they are concealed by opaque organs. Tuberculosis of the tracheobronchial lymph nodes is evident in roentgenograms when caseous material has become partially or completely calcified. Caseous lymph nodes with no calcification are recorded in roentgenograms only when they have undergone massive enlargement. The lymph nodes that are the sites of visible tuberculosis are found at the hilum of the lung in contact with the larger bronchial trunks, below the bifurcation of the trachea, where the largest lesions are found, and on one or the other side of the trachea, being usually more conspicuous on the right. Masses below the bifurcation of the trachea are occasionally from 2 to 5 cm. in diameter. Dense, sharply defined opacity suggests that calcification is advanced, whereas shadows of less density occurring in small spots, which give a granular appearance to the lesion, suggest the early stage of calcification. The associated pulmonary lesion is often invisible, being small or behind an opaque organ; but in more than half of the instances in which tuberculosis of tracheobronchial lymph nodes is evident a calcified nodule or, less frequently, the shadow of diffuse infiltration is seen in the lung field nearby. Almost always these lesions are smaller or less conspicuous than those of the tracheobronchial lymph nodes, and for this reason are less frequently recorded in the roentgenogram. Calcium deposited in caseous material casts a conspicuous shadow on the film even though the caseous material, as can be shown at autopsy, is putty-like and contains no solid particles. Calcification recognizable in roentgenogram does not prove that the lesion is arrested, for observations made postmortem have repeatedly shown that the disease may be progressive in the lung even though the lymph node is the site of calcium deposit, and that tuberculosis of the lymph nodes may be progressive even though foci of calcification occur within them. Small caseous lymph nodes are not recognizable in roentgenograms of the chest, but massive tuberculosis of these organs may cause such enlargement and opacity that their rounded outline is distinctly recognizable. The shadow of the structures at the hilum tends to obscure them, but when they project into the clearer lung field their outline becomes visible. In roentgenograms, tuberculous infiltration of childhood type presumably caused by tuberculous bronchopneumonia with subsequent tubercle-formation is usually recognized as a soft, ill-defined, occasionally flocculent opacity in any part of the lung field. It is sharply limited only when it comes in contact with an interlobar surface. Dense opacity indicates that pneumonic consolidation, presumably with some caseation, has affected a wide area of lung substance. The centre of the abnormal shadow is a dense homogeneous opacity, which decreases at the margin, becomes more or less irregular, and disappears into the normal lung field. In older children, usually after 14 years of age, recognizable tuberculous lesions in the lung fields are usually strand-like and contain calcified nodules. Even though there is an active tuberculin reaction, such lesions are doubtless in most instances arrested. In twenty-five among 45 instances of the childhood type of pulmonary tuberculosis, both latent and manifest, tuberculosis of tracheobronchial lymph nodes was sufficiently conspicuous to be recognizable in roentgenograms. Apical lesions when least conspicuous appear as soft shadows or mottling below the border of the second rib. Wedges or salients projecting downward in this position are not infrequently seen. Sharply defined strand-like shadows in the apex suggest that the lesion is in the process of healing, but this evidence is uncertain and repeated examinations are essential to exclude the possibility that the lesion is progressive. Among 31 instances of pulmonary tuberculosis of adult type, clinically manifest and latent, tuberculosis of the tracheobronchial lymph nodes was recognized in thirteen, and in nearly all of these a calcified nodule

was found in the lung field nearby. Animal experiments and some clinical observations show that sensitization to tuberculin may disappear after complete recovery from tuberculosis. A few school children with calcified nodules in the lungs and adjacent lymph nodes have failed to react. The intensity of the tuberculin reaction has considerable significance. All instances of clinically manifest tuberculosis among school children occurred in those who reacted to 0.01 mgm. of tuberculin, and in two-thirds of these the reaction was three plus. With few exceptions, children with latent infiltration of childhood type reacted to the same amount, and in considerably more than half of them the reaction was three plus. Loss of weight cannot be used as an index of tuberculous infection until the disease is so far advanced that it has undermined health. Among 44 school children with the childhood type of tuberculosis, both clinically manifest and latent, overweight was just as frequent as underweight. Among 20 school children with the adult type of tuberculosis, both the clinically manifest and latent apical, the weight was slightly below normal in fifteen and materially diminished (more than 10 per cent of normal) in five. Study of the contagion of tuberculosis in families made during the last six years has shown that a large percentage of all instances of advanced tuberculous infection occurs in persons known to have been exposed to open tuberculosis within the family group. In these families at least 9 per cent of the children develop clinically manifest disease; many develop latent infiltrating lesions of childhood or lesions of adult type, and tuberculosis of tracheobronchial lymph nodes is found in approximately one-fourth of them. The transition from grave latent lesions to clinically manifest disease has been repeatedly followed. Advanced tuberculous infection, for example, massive tuberculosis of tracheobronchial lymph nodes, indicates that the child has received tubercle bacilli in large number. If this exposure continues, reinfection may result and the adult type of pulmonary tuberculosis makes its appearance. Intracutaneous tuberculin tests made on 4,000 school children from 1926 to 1929 in Philadelphia show that 37 per cent of the children are infected at 5 years of age, 71 per cent at 10 years, 80 per cent at 15 years, and 90 per cent at 18 years. Aronson has found that approximately 25 per cent more school children react to the intracutaneous than to the Pirquet test. Demonstrable tuberculous infection with the following characters is prevalent among healthy children and requires no special care to prevent its further development: (1) infection revealed by the tuberculin test with no lesion demonstrable by roentgenological examination; (2) circumscribed pulmonary nodules that have undergone calcification; (3) roentgenographically demonstrable tuberculosis of tracheobronchial lymph nodes, with the exceptions to be cited. Children with the following conditions are in danger of tuberculosis that will undermine health and should receive special care in open-air schools or preventoria: (1) latent tuberculous infiltration of the childhood type evident in roentgenograms, often associated with tuberculosis of tracheobronchial lymph nodes; (2) tuberculosis of tracheobronchial lymph nodes with some calcification, recognizable by roentgenological examination, (a) when the child is still in contact with open tuberculosis, (b) when the tuberculin reaction is intense, (c) when the lesions are unusually large or very numerous; (3) latent tuberculosis of adult type; (4) arrested pulmonary tuberculosis, notable in children who have been discharged from sanatoria; (5) an active tuberculin reaction or an otherwise negligible tuberculous lesion recognized by roentgenological examination in association with impaired health and conspicuous underweight. Children who should receive sanatorium treatment or its equivalent are (1) those with tuberculous lesions accompanied by symptoms and physical signs referable to tuberculosis; (2) those with latent lesions of the lung either of childhood or adult type that on repeated roentgenological examination are found to be progressive; (3) those with massive tuberculosis of tracheobronchial lymph nodes that have not undergone calcification. In the search for tuberculous infection, two procedures are available: (1) examination by tuberculin tests and roentgenological examination of all children known to be exposed to open tuberculosis, a method that would be effective in proportion to the success of tuberculosis registration; and (2) roentgenological examination of school children who react to tuberculin, precedence being given to groups of children, such as adolescent girls and Negro children, among whom the disease is known to be unusually frequent.—*The Significance of Advanced Tuberculous Infection of School Children, E. L. Opie, J. Am. M. Ass., October 18, 1930, xcv, 2151.*—(*G. L. L.*)

Tuberculosis in Schools in Colorado.—This is a study of 283 children in the town of Aurora, Colorado, whose total population is 968. The town contains the largest institution in the United States caring for tuberculous patients, so that a large proportion of the population consists of health-seekers and tuberculosis-contacts. The children studied were from four to fifteen years of age.

Tuberculin tests gave positive results in 103 children, or 36.4 per cent. of the whole group. The Mantoux (intracutaneous) and Craig (multiple-puncture) tests gave practically identical results, reactions to the former, however, being invariably larger. The number and size of positive reactions increase in children commensurately with contact and age. The incidence of tuberculous infection among children varies greatly in different parts of the country, and is influenced by climatic and other environmental factors. In this community, with so high a contact-rate, the incidence was only slightly greater than that noted in nontuberculous communities. Roentgen studies of the 103 children giving positive reactions revealed childhood tuberculosis in 19, or 6.7 per cent. of the whole group, the average for the country at large varying from 1 to 4 per cent. No child with the adult or exudative type of tuberculosis was found. Most of the children reacting positively and those having actual childhood tuberculosis were not born in Colorado. Climatic conditions in Colorado apparently exert a favorable influence in the protection of children against active tuberculous infection. In this study, the father was the source of infection in 64.8 per cent of the children giving positive reactions, and the mother in only 12.6 per cent. Symptoms of fatigue, undernutrition, and a history of frequent colds, are not reliable aids in the diagnosis of childhood tuberculosis.—*A Survey of Tuberculosis in Schools in Colorado, R. P. Forbes, R. Verploeg and M. K. Bazemore, Am. J. Dis. Child., January, 1931, xli, 26.*—(*P. J. W.*)

Tuberculosis in Childhood and Adolescence.—Statistical studies demonstrate that under conditions of domiciliary infection, infants are most susceptible to tuberculosis, that the susceptibility decreases in early childhood, and more so in the age-group of 6 to 10 years. An infection acquired in prepuberty may lead to disease after years. The frequency of exposure cannot *per se* explain the characteristic curve of tuberculosis mortality from infancy to adolescence; it is necessary to assume a difference in susceptibility at various ages, a susceptibility which is a function of age. The various types of the disease which predominate in various age-groups would argue in favor of the same concept. Hilar tuberculosis, essentially a disease of lymphoid tissue, is predominant in infancy and childhood; haematogenous propagations are most frequent in later childhood, while localized pulmonary lesions make their appearance in late childhood and adolescence. There seems to exist a parallelism between the physiological lymphocytosis of childhood and the preponderance of lymphoid localization. The curve of the tuberculosis mortality shows the same trend as that of the total mortality. The varying tuberculosis susceptibility at different ages indicates upon which age-group prophylactic measures must be concentrated.—*Über Altersdisposition zu Tuberkulose in Kindheit und Jugend, J. Peiser, Klin. Wchnschr., January 10, 1931, x, 77.*—(*M. P.*)

Symptoms and Signs in Suspected Juvenile Tuberculosis.—A clinical and roentgenological study of 306 cases of suspected juvenile tuberculosis was made, with special reference to the evaluation of 9 clinical symptoms, 10 clinical signs, 9 roentgen observations, and the tuberculin test. Two hundred and six patients gave positive tuberculin tests, and 100 patients negative. The symptoms considered were repeated diseases of the upper respiratory tract, cough, nervousness, lack of appetite, loss of weight or failure to gain, fatiguability, night-sweats, lassitude, and elevation of temperature. In group I (tuberculin-positive), 75 patients (36.4 per cent) presented no symptoms. In group II (tuberculin-negative) 42 patients (42 per cent) presented no symptoms. Cough was noted in 41.8 per cent of group I and in 55.2 per cent of group II; and nervousness in 41.8 per cent of group I, and in 39.6 per cent of group II. Lack of appetite and loss of weight were next in frequency in other groups. The physical signs recorded were d'Espine's sign, paravertebral dulness, malnutrition, dulness of the *manubrium sterni*, enlargement of the cervical lymph nodes, abnormalities of percussion and auscultation, phlyctenular processes, involvement of bones, and indications of tuberculous adenitis. In the tuberculin-negative group, 11.2 per cent, and in the tuberculin-positive group, 12 per cent., presented no clinical signs referable to tuberculosis. The first four signs occurred most frequently in both groups, in the order named. Roentgenographic observations recorded were hilum calcifications, increased lung markings, enlargement of bronchial lymph nodes, calcification of bronchial lymph nodes, thickening of interlobar pleura, peribronchial infiltration, primary focus, and parenchymal tuberculosis. In group I, 5.8 per cent presented no positive X-ray findings, as compared with 15 per cent in group II. X-ray findings occurring more often in group I than in group II were hilum calcifications, increased markings, and thickened interlobar pleura. Peribronchial infiltration was found oftener in group II than in group I; and the remainder of the roentgen findings about equally often in both groups. Thus it would seem that the commonly accepted clinical

symptoms and signs have no diagnostic significance, except as they may be correlated with roentgenograms and the tuberculin test, when these are definitely positive for tuberculosis. Only roentgenograms in conjunction with tuberculin tests were of definite diagnostic value.—*Suspected Juvenile Tuberculosis Evaluation of Clinical Symptoms and Signs, F. Eberson, J. P. Delprat and E. Wolff, Am. J. Dis. Child., October, 1930, xl, 753.—(P. J. W.)*

Effect of Nonspecific Factors on Tuberculin Skin Reaction.—About 5,000 tests were performed on about 1,000 patients, who were studied during both the acute and the convalescent stages of disease, the entire study covering a period of two years. There is often a depression of skin response to tuberculin in acute diseases. During the acute stage of such diseases as measles, diphtheria, scarlet fever, and other acute conditions accompanied by febrile reactions, the tuberculin test, which had previously been positive, may become negative, returning to positive again during convalescence. This is shown by the fact that 11 of 16 children who were known to have positive tuberculin reactions had no skin response to tuberculin during acute febrile illness. It is further supported by the fact that, of 159 children who had positive tuberculin reactions during convalescence from acute diseases, only 49 had positive tests during the febrile stages of these diseases. Stated otherwise, of 934 patients, 49, or 5 per cent, had positive tuberculin reactions during the acute febrile stages of various diseases, and 159, or 17 per cent, of these same patients had positive reactions during convalescence. All of the 49 who had positive reactions during the acute stage also had positive ones during convalescence. The depression of response does not seem to be peculiar to any disease or diseases, but depends rather on the severity and on the fact that fever is present. That this is a depression but not an absence of response seems likely, because a positive skin reaction may be obtained by injecting a larger dose of tuberculin during the acute stage than is necessary to cause a reaction during convalescence. The skin response to tuberculin may be delayed for several days.—*Studies in Immunity: II. The Effect on the Skin Tuberculin Reaction of Non-Specific Factors, B. Eddy, and A. G. Mitchell, Am. J. Dis. Child., October, 1930, xl, 771.—(P. J. W.)*

Friedmann's Vaccine in Children.—In 1927, eleven tuberculous children were treated with Friedmann's vaccine. The children were selected by Friedmann himself, who determined the mode of application and the amount of the vaccine. Friedmann reëxamined the children thirteen days after vaccination and found "some improvement." At the end of seven months of observation after treatment, it was found that seven of the eleven had fistulous tracks from the site of inoculation. These finally healed, except in two cases. Of the 11 children, five improved, four showed no change and two experienced progress of the disease. The group that improved comprised one instance of tuberculous ulcer, three of cervical adenitis (one of which had an epituberculous infiltration), one tuberculous peritonitis, one tuberculosis of elbow and knee. When seen three years after the treatment, it was noted that some of those who had improved early were worse and one who had progressed at first showed improvement. It is concluded that treatment with Friedmann's vaccine in these 11 children produced no demonstrable influence on the clinical course.—*Therapeutische Versuche mit dem Friedmannschen Tuberkuloseimpfstoff bei Kindertuberkulose, H. Fernbach, Deutsche med. Wchnschr., August 1, 1930, lvi, 1295.—(H. S. W.)*

Enlarged Cervical Lymph Nodes in School Children.—In the majority of children during school age there occurs especially on the left side, palpable cervical lymph nodes which become less frequent after the tenth year and are only occasionally seen after the 13th and 14th years. The author examined 100 school children of various ages to determine the aetiology of these enlarged nodes, and in only 50 per cent was there a positive biological reaction to indicate that the tubercle bacillus was not the occasioning factor and it is believed that other infectious agents account for this as well as a certain amount of lymphatic diathesis.—*Stehen die Halsdrüsenschwellungen der Schulkinder in Beziehung zur Tuberkulose? G. Poelchau. Zeitschr. f. Tuberk., 1930, lv, 483—(H. J. C.)*

Epituberculosis.—Ten typical cases of epituberculosis in children were studied clinically and roentgenologically for about two years. All were tuberculous children who presented massive pulmonary involvement, which either completely disappeared or is still undergoing resolution. In one of the cases which had resorbed an infiltration of the right lung followed a tuberculin reaction. The epituberculous infiltrate is intimately associated with reactions of the tubercle bacillus or of its toxins. It is not clear whether the epituberculous area is a collateral inflammation or an atelectasis, the result of blockage of an enlarged hilum lymph-node process, or a truly tuberculous parenchymal involvement, or any of these in

a given case.—*Epituberculosis. A Study of Ten Cases for a Period of over Two Years, B. Goldberg and B. M. Gasul, Am. J. M. Sc., December, 1930, clxxx, 824.*—(*W. I. W.*)

Serofibrinous Pleurisy in Childhood.—The serofibrinous pleurisies are commoner in later childhood than in infancy. Of 38 cases, 34 were in children over three years of age. Among boys and girls the incidence was about equal. No significant difference has been found between the sides of the chest, as regards susceptibility to pleurisy. In all of the 38 cases studied in which the tuberculin skin-test was done, it was found positive. In spite of their tuberculous origin, the serofibrinous pleurisies recover well and rapidly. In only two cases was the pleurisy followed by pulmonary tuberculosis. The amount of the effusion is almost always small. Only very seldom need thoracentesis be performed, this procedure ordinarily doing more harm than good; yet exploratory puncture may be necessary to determine the nature of the effusion. Rest and the usual hygienic measures should be employed, with heliotherapy during convalescence.—*Notes sur la pleurésie séro-fibrineuse infantile, J. Comby. Arch. d. Méd. d. Enf., January, 1931, xxxiv, 1.*—(*P. J. W.*)

Tuberculosis in Mesenteric Lymph Nodes of Children.—In a series of 161 children under 15 years of age, dying of all causes, there was anatomical evidence of tuberculosis somewhere in the body in 50 cases. Twenty-two of the children were under two years of age. In 28 cases tuberculosis was considered the primary cause of death. In 19, evidence of generalized miliary tuberculosis was found; in 11 there was tuberculous meningitis; and in 7, tuberculous peritonitis. There was caseation of the mesenteric lymph nodes in 15 of the patients dying of generalized miliary tuberculosis, and in only 3 was there any calcification of these nodes. Forty-five cases gave evidence of tuberculosis in the mesenteric lymph nodes, 27 showing caseation, 11 caseation and calcification, and 7 calcification without caseation. Five of the 18 with calcified mesenteric nodes were children under 2 years of age, the youngest being 6 months old. All 4 of those between 14 and 15 years of age had calcification of the mesenteric nodes. The remaining 8 with calcification were between 2 and 14 years of age. In 18 cases, tuberculosis of the mesenteric nodes was the only demonstrable tuberculous infection in the body. In no other tissue was the incidence of tuberculosis comparable with that in the mesenteric nodes. Pulmonary tuberculosis was found in only 25 cases, in 20 of which there was also tuberculosis of the mesenteric nodes. The tracheobronchial nodes were the site of tuberculous infection in only 22 cases, in 18 of which there was tuberculosis of the mesenteric nodes. Tuberculous enteritis occurred in 20 cases, in 17 of which there was coincidental involvement of the mesenteric nodes. In all tissues other than those mentioned, tuberculosis was found in 31 cases, and in 26 of these tuberculosis of the mesenteric nodes was present. The fact that in 18 instances, or over one-third of the cases studied, the mesenteric nodes were the only tissues in which tuberculosis was found, indicates the importance of the intestinal lymphatics in the infection of children with tubercle bacilli.—*Tuberculosis in the Mesenteric Lymph Nodes of Children, M. Leonard, Am. J. Dis. Child., March, 1931, xli, 513.*—(*P. J. W.*)

Erythema Nodosum in Children.—Erythema nodosum may occur in nontuberculous individuals or in those infected with the tubercle bacillus. In a great majority of cases erythema nodosum in children is associated with tuberculous infecton and most of these infections are initial and recent. Most children who have erythema nodosum exhibit marked hypersensitiveness to tuberculin given intracutaneously. There may be associated, in addition to the tuberculous infection, other conditions which possibly influence the hypersensitiveness to tuberculin. In many cases of erythema nodosum in children epituberculous lesions in the pulmonary parenchyma can be demonstrated by roentgenograms of the chest. In the series reported none of the individuals observed was known to develop a very active tuberculous lesion of the lung. The lesions of erythema nodosum, the epituberculous lesions and the positive skin tuberculin reactions are similar histologically. As erythema nodosum is usually associated in children with early tuberculous infections, proper treatment for the latter condition gives a favorable prognosis as far as tuberculosis is concerned.—*The Etiology of Erythema Nodosum in Children. Its Relation to Early Tuberculous Infections, L. B. Dickey, Am. J. M. Sc., October, 1930, clxxx, 703.*—(*W. I. W.*)

Acute Generalized Tuberculosis without Typical Tubercles.—A female infant was first examined at the age of 10 weeks because of an ulcer of the buttock of two weeks' duration. She had spent the first two weeks of her life with her maternal grandmother, who had "chest trouble," not diagnosed as tuberculosis. The baby was poorly nourished. During the last three

weeks of her life her temperature varied from 101° to 104°F. She died at the age of three months. Three weeks before her death, X-ray revealed a pulmonary process similar to miliary tuberculosis, but with larger shadows. The intracutaneous tuberculin test was negative. Tubercle bacilli were found in the gastric contents four days before death. Autopsy revealed a large caseous mass in the upper lobe of the right lung, without typical tubercles. Stains for tubercle bacilli showed many organisms. There was no typical tubercle-formation in the nodules found throughout the rest of the lung (also in liver and spleen). In the centre of each nodule was an area of acute necrosis, which stained slightly pink and was infiltrated with polymorphonuclear cells. An occasional cell resembling an epithelioid cell was seen, but these were very few. There were no giant cells. Farther out from the centre of each nodule, many polymorphonuclear cells were found. Stains made of the nodules for acid-fast organisms showed a tremendous number of tubercle bacilli. Many organisms were also found in the ulcer on the buttock, but no typical tubercles. Among others, Krause is quoted to the effect that "Epithelioid cell is pathognomonic of tubercle. Tubercle bacilli alone may be present in a lesion; even then it is not a tubercle; nor is it one if lymphocytes alone display themselves, or giant cells alone." The microscopic appearance of the lesions in this patient is probably due to two causes: (1) the lack of allergic response as judged by the negative skin reaction to tuberculin, and (2) the lack of resistance, which was shown by the tremendous number of organisms in each lesion. Although bacilli are transported by the blood-stream, a resistant patient does not allow the multiplication of these organisms. A more resistant patient also reacts by the formation of typical tubercles.—*Acute Generalized Tuberculosis without Typical Tubercles, W. A. Reilly and Z. E. Bolin, Am. J. Dis. Child., March, 1931, xli, 582.*—(*P. J. W.*)

Report of Committee on Tuberculosis of American Veterinary Medical Association, 1930.—The work of eradication of tuberculosis in the United States continues apace. Of 3,072 counties, 962 are classified as modified accredited areas. Area work is being done in 1,413 counties at present. Modified accredited areas are now present in 38 states. Michigan, this year, joined two others in becoming completely accredited. The total number of herds tested during last year was 1,102,243. This comprised 12,845,871 cattle. In Canada, gratifying progress is being made. The farmer and dairyman are demanding area testing. One-eighth (1,500,000) of Canadian cattle have been tested once. Two hundred and nine provinces are now "restricted areas." The work is entirely Federal and, therefore, it proceeds more slowly without state coöperation. In the United States and Canada, there still exists some doubt among the farmers as to the advantage of tuberculin testing, as to whether tuberculin is a poison, and as to whether tuberculin testing may not lead to many mistakes. Therefore, the committee has prepared a definitive statement on this subject. *BCG* has come in for extensive study in recent years. Several studies indicate that 61 per cent of the cattle previously inoculated with *BCG* and then exposed to tuberculous cattle developed tuberculosis which was proved at autopsy, while 87 per cent of unvaccinated controls developed the disease. This means that 25 per cent of the animals vaccinated with *BCG* were better off than those not so vaccinated. Protection by inoculation with *BCG* tends to be lost with the passage of time and it sometimes totally disappears in spite of reinjection of the product. Some work indicates a large percentage of protection in the first year of *BCG*. At best, it seems capable of only *delaying* the development of tuberculous infection or of *retarding* tuberculous disease. Aside from the questionable efficacy in preventing tuberculosis, potent dangers in its application must be considered. Virulent tubercle bacilli have been recovered from the lymph nodes, milk and vaccinal focus of animals vaccinated with *BCG*. Cattle vaccinated with *BCG* and then exposed to tuberculosis sometimes become carriers of virulent bacilli. Caution, reservation and further experiments are still necessary before definite conclusions can be deduced. Avian tuberculosis has likewise come in for considerable notice during recent years and is now much more recognized as an important factor in the question of eradication. The following facts may be stated (1) 88.5 per cent of the localized tuberculosis in swine in some localities is due to avian bacilli, (2) less than 1 per cent of eggs laid by tuberculous hens contain tubercle bacilli, (3) baby chicks are not hatched with tuberculosis, (4) avian bacilli remain viable after two years in barnyard soil, (5) rats, pigeons and sparrows are carriers, (6) the minute dose of 0.000001 mgm. is sufficient to sensitize a fowl to tuberculin. These are some of the important data on which eradication of this type of tuberculosis is based. The committee has recommended that the American Association of Medical Milk Commissioners appoint a committee to confer with a similar committee from the American Veterinary Medical Association on the ques-

tions regarding tuberculin testing, certified milk, etc. The questions of the merits of pasteurization versus certified milk are still important.—*Report of Special Committee on Tuberculosis, J. Am. Vet. Med. Ass., October, 1930, lxxvii (n. s. xxx). 507.*—(*H. S. W.*)

Legal Aspects of Tuberculosis Eradication in Cattle.—Both federal and state laws have been passed to regulate the eradication of tuberculosis from cattle. The provision for the federal share of indemnity has been established at $25 to $35 per head for grade cattle and $50 to $70 for pure-bred cattle. State legislation has been varied but, in general, remarkably successful. This is especially true for the regulations concerning area-testing and accrediting. Municipal ordinances regulating the source, handling and distribution of milk have helped greatly in the control of bovine tuberculosis in human beings. Several instances have arisen which have tested and vindicated the laws through law suits.—*Legal Aspects of Tuberculosis Eradication, A. E. Wight, J. Am. Veterin. Med. Ass., July, 1930, lxxvii (n. s. xxx), 18.*—(*H. S. W.*)

Subcutaneous Tuberculous Lesions in Cow.—A case-report carries the description of subcutaneous nodules from one-half to one inch in diameter on the leg of a cow. They were numerous, firm, but movable and extended along the lymphatic vessels of the part. The cow failed to react to intracutaneously administered tuberculin, but did react to intravenous injection of avain tuberculin. Biopsy of a nodule revealed a few acid-fast bacilli, which led to "mild" disease of the liver and spleen when inoculated into guinea pigs They led to no disease in fowl. The nodules were excised. A second cow presented similar lesions which contained acid-fast bacilli that could not be proved to be pathogenic.—*A Note on Subcutaneous Tuberculous Lesions, R. Graham, F. Thorp and W. A. James, J. Am. Veterin. Med. Ass., July, 1930, lxxvii (n. s. xxx). 97.*—(*H. S. W.*)

Pulmonary Lesions in Avian Tuberculosis.—Avian tuberculosis is supposed to spare the lungs generally, or to involve the abdominal viscera to a much greater extent than the thoracic viscera. Autopsy on 49 hens with tuberculosis revealed disease in the lungs and pleura in 45 per cent; of the intestines in 59 per cent; in the liver in 89 (plus) per cent; in the spleen in 61 per cent, with a small percentage of other studies involved. The hens had been housed in a building that had not been cleaned for months. Clouds of (contaminated?) dust arose during the scratching incident to feeding and this is presumed to be the source of the pulmonary disease.—*Lung Lesions in Avian Tuberculosis, L. R. Vawater, J. Am. Veterin. Med. Assoc., July, 1930, lxxvii (n. s. xxx), 103.*—(*H. S. W*).

Expermental Tuberculosis of Horse.—*Histogenesis of Tubercle Constituents:* So rarely is spontaneous tuberculosis met with in the horse that each case observed is often the subject of record of discussion. Vallée and Panisset cite German statistics of frequency, according to which about one animal is affected in 5000. In Paris the figures indicate only one case to 15,000 animals. In England and Denmark the disease is more frequent, because of the fact that in these countries colts are brought up on cows' milk. Pickens, in a study of 54 cases, found the spleen most frequently affected (on 70 per cent) and next to this the lungs and mesenteric lymph nodes. The portal of entry, according to Vallée, is the digestive tract, whence the bacilli reach the thoracic lymph nodes. To this viewpoint there is one difficulty, the absence of lymphatic connections between the thorax and abdomen. Man and cattle seem to differ from most animals in having the respiratory passages the ordinary site of election of primary infection. The development of equine tuberculosis is slow and its duration long. *Spontaneous Pulmonary Tuberculosis in the Horse*: The clinical symptoms are not particularly striking, consisting chiefly in a dry cough, a dyspnoeic respiration and, quite late, positive auscultatory signs. There are two principal forms of pathological lesions, the first consisting of nodular tumors the size of a nut up to that of a man's fist, in the midst of thick connective tissue, and containing a caseous mass; the other type has a structure rather resembling a sarcoma, without caseation or surrounding inflammation. These lesions have been studied by Steffens, who believes that the primary effect of the tubercle bacillus is either an interstitial inflammation or alveolitis. Often the two forms exist simultaneously. Miliary foci are usually of the neoformative type. Where the exudate reaction is most marked there are apt to be the most bacilli and toxins, while where the bacilli are sparse the neoformative reaction predominates. The serous membranes, especially the pleura, are rarely involved; when they are, it is the proliferative type, the surfaces being covered with nodules in the centre of which there is necrosis. The concretious characteristics of bovine tuberculosis do not develop. Often there are to be seen simultaneous lesions of the lung and tracheobronchial lymph nodes. The latter are hyperplastic but macroscopi-

cally normal. The associated lymphatic lesions are important because in certain pseudotuberculous parasitic conditions they are always absent. The tracheobronchial mucosa is uninvolved up to the interlobular ramfications, and only exceptionally are the pulmonary vessels affected and then secondarily. *Experimental Pulmonary Tuberculosis:* The horse, generally refractory to tuberculosis, has rarely been used experimentally. However, Gabriel Petit, Panisset and Kfourg did succeed in producing a tuberculosis of slow development, confined almost entirely to the lungs. Their technique recalls that successfully employed by Herxheimer in 1903 on rabbits and guinea pigs, Calmette and Guérin in 1906, and more recently by Gross in 1926 on rabbits, using a combination of tubercle bacilli and mineral dust. Through a tracheotomy opening a fine flexible sound is introduced to a depth of 80 to 100 cm., and then, by means of a glass syringe, the bacillary emulsion, diluted with physiological salt solution, is introduced. Petit, Panisset and Kfourg studied its progression and distribution in living animals with the aid of lipiodol and the X-rays, and on the necropsy table by injections of methylene blue. Narcosis is not indispensable but renders the injection easier. They have found that canine tuberculosis, thus induced, develops surely but slowly and without marked clinical manifestations, but that after a few weeks the tuberculin test and serum reactions are positive. The anatomical lesions take the form of caseous pneumonia with softening, resulting sometimes in a spontaneous pneumothorax. The lesions resemble those in human beings. In the rabbit the disease may take three months to develop, although Gross found a specific pneumonia at the end of one month. Herxheimer noted a catarrhal alveolitis within forty-eight hours and after six weeks a proliferative pulmonary tuberculosis. Attempts at endobronchial infection of horses by Zahrzewski gave satisfactory results. Of four horses tuberculized toward the end of 1925, 3 remained in good health, the other died a year later and its lungs constitute the subject matter of this paper. *Clinical and Necropsy Findings*: The animal was a half-blood, about 15 years old, weighing at the beginning of the experiment 460 kg. Before her death, hastened by a copious haemorrhage, her weight had dropped to 410 kg. She received human bacilli from Calmette's laboratory. The emulsion was obtained by diluting 10 mgm. of bacilli in 1 cc. of physiological salt solution. A flexible filiform sound was introduced, followed by a tracheotomy tube. Four doses of infection were given as follows: November 10, 1925, 30 mgm.; January 23, 1926, 90 mgm.; March 19, 1926, 150 mgm.; and May 22, 1926, 300 mgm. This gives a total of 570 mgm. of bacilli in six months. After each injection a rise of temperature was noted, occurring between 24 and 36 hours. The second month after the inoculation the tuberculin test was positive; likewise the complement fixation reaction with the Boquet-Nègre antigen. Examination of the mare's organic fluids and excretions revealed no bacilli, and guinea pigs and rabbits inoculated with them remained healthy. Finally, there was noted a zone of dulness on the right side and occasional mucous and sibilant râles. The animal's respirations became sighing and dyspnoeic. Cough appeared after the third inoculation and persisted. At necropsy there were seen on the internal surface of the left lung, at the junction of the tracheal and principal lobes, multiple caseous nodules, about 1 to 1.5 cm. in diameter. The surrounding parenchyma was inflamed, dense, sclerotic and hyperaemic. The pleura was intact. Certain foci, more or less confluent, surrounded important bronchial or vascular ramifications. The internal border of the right lung revealed a conglomeration of nodules, 5 to 10 cm. in thickness, enmeshed in subacute inflammatory tissue. There was also at the diaphragmatic margin a nodule of considerable size, completely caseous and soft. The azygos lobe was hypertrophied and abundantly covered with caseous tubercles. Certain tracheobronchial lymph nodes were adherent and enlarged and continued caseous foci. All the other organs were intact. It was concluded that experimental endobronchial tuberculous infection provokes a morbid state approaching that seen in spontaneous tuberculosis in man. On the other hand, the tuberculosis developing after intravenous injection leads to death within three months at the most, with generalized miliary lesions. *Results of Histological Studies*: Eight sections were removed from the left lung, in which the most fully developed and varied lesions were found, from miliary foci to more voluminous nodules, and large caseous nodules; also small subpleural foci. From the right lung five sections were taken, showing apparently inflammatory foci, surrounding miliary nodules already undergoing caseation and situated near the bronchi, larger foci between them,a portion of a caseous focus and finally a piece of emphysematous parenchyma from the apical region. The hilum lymph nodes, on section, seemed intact. The following stains were used: Schmorl's modification of the Ziehl-Neelsen, Van Giesen's, Mallory's Weigert's, orcein, resorcin-fuchsin, and haematoxylin-eosin-orange. It was established

that only the young foci or those undergoing mortification, are entirely deprived of bacilli. The bronchi and blood-vessels showed hardly any, and only once were they found in the foci of specific exudative pneumonia. They were numerous in the middle of old necrotic masses, and fewer toward the centre and periphery. The number found seems small in comparison to the myriads introduced. Even where most frequent they did not exceed 20 per microscopic field. Their form varied, most frequent being those with 3 to 5 small linear nodosities, corresponding to Much's granulations. Reasons for their disappearance may be (1) long exposure to formalin, which however Petit found not to affect coloration; (2) destructive action of the fatty-waxy capsule, due to specific resistance of the horse; and (3) presence of an invisible filterable virus. Sections from the horse infected intravenously failed to show any bacilli. The pleura was almost intact, showing merely a slight thickening in the neighborhood of subjacent foci. The intralobular bronchioles were somewhat thickened, their lumina containing debris from epithelial desquamation, also much mucus and polynuclear leucocytes. The vascular system was considerably involved: the venous ramifications of the interlobar septa were often dilated, filled with blood or thrombi. The smaller vessels on the surface of the tuberculous foci showed a proliferative vascularitis, with stenosis or obstruction. Due to the thickening of interalveolar and interlobar septa numerous alveoli were obliterated and contained cellular debris or oedematous exudate. To sum up, those parts of the lung specifically affected showed a chronic oedema, a partial atelectasis, and a variable degree of emphysema. The tuberculous lesions were composed principally of granulations with central necrosis, a double layer of epithelioid cells and lymphocytes, and a connective-tissue envelope. The youngest tubercles were made up of epithelioid cells, with here and there lymphocytes or leucocytes. The centre of the granulations showed sometimes distended capillaries but no giant cells. A thin ring of cells and connective-tissue fibres were arranged concentrically about it. The peripheral pulmonary parenchyma showed hardly any reaction or a slight infiltration of mononuclears. The larger foci were granular,—what Letulle, following Laennec, describes as "*granulatio miliaris.*" The largest granulations showed central necrosis surrounded by concentric rings of epithelioid cells. Among them were occasional atypical giant cells. The oldest foci showed necrotic masses with dry walls but no calcification. The fibrous capsule had become well developed and contained certain neovascular nodosities. A second type of lesions consisted of inflammatory foci which one might identify as Virchow's "caseous desquamating pneumonia," or Letulle's "lobular bacillary pneumonia." Lobules showed different degrees of alveolitis,—simple, serofibrinous, or necrosing. Recent lesions showed alveoli distended with serum, in the neighborhood of others filled with cellular debris or with erythrocytes. The older foci contained only fibrin, lamellated rather than filamentous, and strongly acidophilic, characteristic of inflammatory processes of the lung. At a later stage the alveoli are involved in a caseous necrosis but with little reaction on the part of surrounding tissues. To sum up, these lesions, with the exception of the necrosis, have no specific appearance and resemble those of ordinary inflammatory foci, for which reason Virchow denied their tuberculous nature. The lungs of intravenously infected horses present a very different picture, being densely sown with tubercles, up to a dozen per microscopic field. One tubercle involves about 10 alveoli. They are made up entirely of epithelioid cells with some monocytes. We have here a recent dissemination of multiple nodules caused by a diapedesis of bacilli from the blood vessels of the lung. In its developmental stage, such a nodule possesses two circles, an external and an internal, but the latter is soon destroyed by necrosis while the external becomes more dense and fibrous. In old tubercles the necrosis reaches the external ring, encroaching on the epithelioid and lymphoid zone. The internal ring would appear to be made up entirely of fibres developing *in situ* from the effects of the bacilli and toxins. The epithelioid cells, however, push these fibres peripherally and the tubercle bacilli provoke their hyaline degeneration. Thus, it is not true that the fibrous elements of tubercles are all of "new" formation; this applies only to the external ring. Where there is massive accumulation of infectious material, cellular proliferation, especially epithelioid, seems to occur at once, as Joest and Einshoff showed in guinea pigs; but, where the infection is slight, a fibrous neoproduction may be only local evidence of a tuberculous process. Such a neoproduction, not being specific for tuberculosis, may readily pass unperceived. Finally, the characteristic lesion of chronic human tuberculosis (woody pneumonia) manifests itself principally by an immense increase of elastic-tissue fibres. In the regions involved by specific pneumonia, the connective tissue process is otherwise. There are no internal and external rings because there is no neoformation to push the local fibres peripherally. The inflammatory exudate accumulates in all the free spaces in

the alveoli, and becomes the prey of necrosis, like the alveolar wall. Nevertheless the collagenous fibres which cross the interalveolar septa separating the inflamed from intact territory, stain more intensely than those in the normal parenchyma. The fibres invaded by the specific virus undergo hyaline degeneration. If the virulence of the process diminishes, the connective-tissue cells in the vicinity of the focus determine a neoformation with an external fibrous ring. Mallory's stain does not appear suited to damaged fibres but only to those intact. It does, however, color the younger lesions. The internal and external rings are but feebly stained. In the recent foci of a desquamative pneumonia only a few fibres take the stain, while in the lung of a horse infected intravenously they stain perfectly. Weigert's stain for fibrin does not appear to reveal much in these lesions. The orcein and resorcin-fuchsin methods, on the other hand, are quite useful, as the elastic fibres are attacked last and the progress of destruction can be noted. Either fragmentation or swelling may occur. *Lymphatic Lesions*: In both horses studied the lesions were identical and showed that the tuberculous infection had taken the vascular route. Macroscopically there was slight hypertrophy of the lymph nodes, which in man is the only sign of recent tuberculous infection (Beitzke). Microscopically there was a large number of miliary or submiliary tubercles, the oldest being in the necrotic stage. These were localized in the red pulp, never in the follicles, and consisted almost entirely of epithelioid cells. Lymphocytes were rarely found in the miliary foci. Mallory's stain has shown the intimate relationship between the epithelioid cells and the finest ramifications of the lymphatic system and the absence of relation with the lymphocytes in the adjacent parenchyma. Joest and Einshoff have made similar observations. There were also observed a considerable number of "plasma cells" enclosed in thickened connective tissue outside the specific lesions. *Mechanism of Development of Lesions:* It has been determined that the most important bronchial branches were never involved; hence there is little evidence of a "peribronchial" dissemination. Moreover, the complete absence of lesions in the deeper tunics of their walls is against such a mode of transmission. An interesting fact, on the other hand, was the determination in the midst of necrotic foci of elastic fibres of vascular origin. Are the vessels then the point of origin of pulmonary infections? If so, then the bacilli introduced by way of the air-passages may penetrate into blood-vessels before reaching the bronchioles or alveoli and without injuring the lung (almost inconceivable) and then return to the lung by way of the blood-stream to develop. In such case it seems incomprehensible that no other organs should be involved. We know, definitely, that intravenous inoculation results in acutely developing disseminated disease. The investigations of Gross help to clarify the subject. He introduced tubercle bacilli together with mineral dust into the rabbit's lung by intratracheal injection, and found that the dust was arrested at the bronchioles on that part of their wall which is traversed by a vessel (*vas concomitans*). This, then, is the primary locus of infection. It has already been said that in old necrotic foci, surrounded by a fibrous envelope, two types of lesion can be differentiated: (1) that in which the necrosis attacks new tissue elaborated under the influence of the virus, "tuberculous granulitis," and (2) that in which the necrosis does not obliterate the former lungs topography and develops in a field of specific pneumonia. The proliferative form, granulitis, is most frequent; the exudative focus of bacillary pneumonia is rather rare. Propagation is by direct continuity, newer foci being generally in the neighborhood of older ones. Propagation by bronchial emboli is rather unusual though possible. Secondary infection by the vascular route is most rare. Many vessels are thrombosed or undergo obliterative vascularities. Those in the affected regions were found entirely impermeable. Still, the mare's death was hastened by a copious haemorrhage, doubtless due to the invasion of a large vessel. The only extrapulmonary lesions, in the lymphatic system, were quite recent. *Conceptions of the Histogenesis of Tuberculous Granulitis:* The point of departure of the two principal ideas on this subject is represented by work done in the last twenty years of the nineteenth century, by Baumgarten and Virchow in Germany, by Metchnikoff and Borrel in France. Baumgarten describes the tubercle as a product containing in its centre several giant cells, surrounded by an epithelioid cell layer and outside of that a layer of lymphocytes. Later its centre necroses and a fibrous capsule develops. Special kinds of tubercles may be composed almost entirely of giant cells, epithelioid cells, etc. The latter are derived from local connective tissue cells under the influence of the tuberculous virus. The giant cells are derived from epithelioid cells and the lymphocytic layer from the blood-vessels of the vicinity, which are hyperaemic. The cellular element of specific pneumonic foci is derived from desquamation of the respiratory epithelium, to which are added leucocytes from the blood-vessels. To-day, in Germany, Baumgarten's ideas are almost a dogma. Weigert elaborated somewhat the

theory of development of giant cells from epithelioid cells, believing the nuclei continued to divide while the cytoplasm underwent necrosis, resulting in the Langlans type of giant cell, with multiple peripherally arranged nuclei. Later he granted that a giant cell could result from fusion of epithelioid cells or development of endothelial cells (Watanabe). After being the centre of a rapid multiplication it degenerated, died, underwent caseation and calcification. But later investigators showed it was not entirely dead but contained numerous living centrosomes. Mitotic figures, however, have never been observed during or before giant-cell development. They appear quite late and are absent in exudative tuberculous proccesses. They are absent in canine tuberculosis but present in canine strongylosis. Joest observed beautiful ones in the horse but in the present study they were variable and not characteristic. There seems to be much less doubt as to the connective-tissue origin of epithelioid cells and in Germany there is practical unanimity on this point. Baumgarten's original ideas on the genesis of the lymphoid cells of the tubercle have greatly changed. This layer develops in poorly vascularized areas and without other indications of inflammation. It now seems to be granted that these lymphocytes, or lymphocytoids, may come from wandering connective-tissue cells become fixed in cellular tissues. These are of diverse types,—clasmatocytes of Ranvier, polyblasts, etc. Recently Masson affirmed that all the elements of the tubercle originate in "lymphocytoids" and that the bacillus provokes the appearance of polynuclears in addition to stimulating local connective-tissue cells to develop into epithelioid cells. All of these, according to Masson, are derived from a vasculoconnective reticulum. Metchnikoff and Borrel, on the other hand, believed these elements to be derived from the phagocytes of the blood stream. Calmette and other French authors have followed this conception more or less closely. Camette states that the white blood cell phagocytizes a tubercle bacillus and is in turn phagocytized by an endothelial cell which becomes transformed into a giant cell. The tubercle, he states, is a product of the lymphatic system, the fixed-tissue cells playing no active rôle. Letulle, however, in his last publication, comes back to Virchow's doctrine that the site of election of specific tubercle is always on the vasculoconnective reticulum. Grawitz and his pupils have elaborated still another theory, that the lymphocytoid cells may be derived from transmutation of local elastic and collagenous fibres, which he does not consider deprived of life, but active and capable of multiplying. His experimental work is not very convincing but has been accepted by Robbers who refers to "plasmatic transformation" of elastic and collagenous tissue. According to him, giant cells develop by transformation and fusion of interstitial elements. *Histogenesis of Tubercle Elements Based on Present Study: 1: Epithelioid Cells:* Tubercles of the lungs and lymph nodes in the horse are, when young, made up of these cells, plus a few scattered lymphocytes and leucocytes. These last come from the vessels, which, at least the capillaries, are locally dilated, and there is also a little serous exudate. The lymphocytes and leucocytes are scattered, diffused, not localized to any part of the lesion. No intermediary forms between lympho-leucocytes and epithelioid cells were observed. Apparently the lymphocytes and leucocytes die but are not transformed. Sections studied with Mallory's stain appear to establish the connective-tissue origin of epithelioid cells, as is evident also in preparations stained with haematoxylin eosin-orange. *2: Giant cells:* These were never observed at the onset but appeared after the "two-ring" formation and were generally rare. Several modes of formation seemed possible, both fusion and nuclear division. *3: Lymphocytoid Cells:* The cells situated in the external circle or ring are included in this classification. They appear late and are disposed along with the elastic and connective-tissue fibres, as Grawitz observed. However, their exact genesis seems yet in doubt. *4: Necrosis:* This results from the death of the local connective tissue, epithelioid cells, and rarely white blood cells. It develops slowly and with less softening than in man. It may be termed "fibrinoid necrosis." *Summary: 1:* Infection of the horse by endobronchial injection of emulsions of tubercle bacilli, determines exclusively pulmonary and adjacent lymphatic lesions. *2:* The bacilli are arrested in the region of the bronchial walls (secondary and tertiary respiratory bronchioles) traversed by a small vessel. *3:* The pathological lesions occur in both productive and exudative forms simultaneously, according to the local abundance of the virus. In the horse infected intravenously they were exclusively productive, developed rapidly and led to death. In endobronchial tuberculosis the productive form was still most frequent and the tubercles appeared first in regions slightly hyperaemic. They were composed of epithelioid cells, local connective tissue, and rare leucocytes and lymphocytes. In the intravenous type giant cells were more common and white cells less so. The older tubercles showed central necrosis, which as it progressed was limited by a well-developed fibrous layer. The age of a tubercle may

be estimated by its connective-tissue fibres. Young tubercles have only a thin fibrillar layer of local origin, which later becomes the "inner ring." In older tubercles this necroses while the outer ring increases. Tuberculous necrosis in the horse is always fibrinoid, without softening or calcification. The blood-vessels show proliferative vascularitis or thrombosis and in the region of the lesions are impermeable. Secondary infection is lacking. Letulle's "bacillary lobular pneumonia" is rare. *4:* Secondary invasion is usually by continuity, more rarely by bronchial emboli and still more rarely by the blood or lymph stream. *5:* The epithelioid cells are exclusively of conjunctive-vascular origin in the lung and lymph nodes. Giant cells are formed by fusion of epithelioid cells and possibly by other means. The origin of the lymphocytoid cells is obscure. They appear early and are probably not derived from the blood cells. Transition forms between these and epithelioid cells were not observed. *6:* The lymphocytes and leucocytes play no important rôle in the development of tubercle in the horse.—*Lésions histologiques de la tuberculose pulmonaire expérimentale du cheval et histogenèse des éléments constitutifs des tubercules, A. Zahrzewski, Rev. d. l. Tuberc., October 1929, x, 644.*—(*A. P.*)

Effect of Human Tubercle Bacilli on Pigeons.—Human tubercle bacilli produce in pigeons nonspecific granulations in various organs, and emulsions of these organs are avirulent for guinea pigs. Only with difficulty and early infection can human tubercle bacilli be cultivated from the blood and organs of the infected pigeons.—*Über die Wirkung menschlicher Tuberkelbacillen auf den Taubenorganismus, A. H. Kuschnarjew, Virchow's Arch., 1930, cclxxvi, 95,*—(*H. J. C.*)

Spontaneous Pulmonary Disease In Albino Rats.—The albino rat is susceptible to a chronic and frequently fatal pulmonary disease. A review of the literature shows that there is no one common aetiological agent. *Bacillus actinoides, Bacillus bronchisepticus, Bacillus muris* and a streptothrix have been isolated from rats by previous workers. In this investigation 16 albino rats, obtained from various sources, were studied. The early stage of this disease produces no observable changes in the appearance or activity of the animal. There are snuffles, dyspnoea and torpor in the advanced stage, and the presence of the pulmonary disease at this time can be demonstrated by the X-ray. At necropsy the lungs usually present single or multiple abscesses, distributed throughout one or several lobes. In some instances the arrangement of smaller abscesses about a terminal bronchus simulates bronchiectasis. The older and larger lesions showed a large caseous central area surrounded by a dense fibrous capsule. A gram-negative motile, aerobic bacillus and a gram-positive anaerobic coccus were isolated from each of the 16 animals. From two of the animals, the bacillus isolated conformed to the characteristics of *B. bronchisepticus* and was agglutinated in high dilution by a serum made from a strain of *B. bronchisepticus* isolated from a rabbit. From the remaining 14 animals a bacillus was isolated which corresponds to the characteristics of *Aerobacter cloacae*, except in the appearance of its colonies and in its faecal odor. This organism will be referred to as *Bacillus type 2*. The anaerobic coccus was not identified. Attempts were also made to reproduce the disease. Intratracheal injections of pus taken directly from an abscess produced isolated abscesses resembling the original. To discover if possible the source of the bacteria producing the pulmonary disease two rats were intratracheally injected with pus from the nasal sinus of a rat suffering from snuffles. One of the animals developed a lung abscess. These observations lead to the hypothesis that the sinusitis was the primary infection and that the pulmonary disease was secondary by aspiration. A purulent sinusitis was induced in two normal rats with a mixed culture of the anaerobic coccus, the *Bacillus type 2* and a fusiform bacillus which had been recovered from a previous spontaneous lung abscess in a rat. One animal died after two days and at necropsy the trachea and bronchi were filled with pus and there was extensive ulceration of the bronchi. Intratracheal injection of either the pure culture of the bacillus or the coccus alone did not produce the disease. Intratracheal injection of a mixture of the bacillus and the coccus produced acute pulmonary abscesses which were identical with those occurring spontaneously. The relation of spontaneous disease to experimental tuberculosis was also studied. Ten rats were inoculated in the groin and five intraperitoneally with bovine tubercle bacilli. Two of the first series and one of the second showed at necropsy thirteen months later a pulmonary disease in which tubercle bacilli were present. Cultures from the lesions also showed the presence of an anaerobic coccus and the *Bacillus type 2* in addition to the tubercle bacilli. Five other animals, three of which received injections of tubercle bacilli in the groin and two in the peritoneum developed pulmonary disease which contained only the spontaneous-abscess organisms. In

no cases were tubercle bacilli found alone. *Conclusions: 1:* A number of different types of organisms are capable of producing pulmonary infections in the albino rat, such as *B. actinoides, B. bronchisepticus, B. muris,* and a streptothrix. *2:* In a group 16 rats studied there were present (1) an unidentified coccus, in all cases; (2) an unidentified aerobic gram-negative bacillus in 14 cases associated with the coccus; (3) bronchisepticus associated with the coccus in two cases; and (4) in two others a large fusiform bacillus, which morphologically was identical with the Vincent's fusiform bacillus found frequently in lung abscesses in man. *3:* A symbiosis of the unidentified coccus and the unidentified bacillus was demonstrated by the failure to produce the disease by inoculation of pure cultures of either, while the combined pure cultures produced a lesion identical with the spontaneous disease. *4:* In experiments with tubercle bacilli in albino rats, care should be taken to exclude the possibility of the presence of a coexisting or preëxisting spontaneous lung disease in which the tubercle bacillus may become implanted. —*Etiology of Spontaneous Pulmonary Disease in the Albino Rat, D. T. Smith, N. Bethune and J. L. Wilson, J. Bact., November, 1930, xx, 361.*—(*F. G. P.*)

Constitutional Disposition to Tuberculosis.—The widely different reactions in human beings against an infection with the tubercle bacillus are in part caused by differences in inherited constitution. The constitution may be determined by race, family or the individual. An example of relative racial immunity is the low tuberculosis mortality of Jews. Racial mixture increases the susceptibility to tuberculosis. The greater frequency of tuberculosis within tuberculous families may be due to the greater danger of infection, but the fact that members of the same family frequently develop tuberculosis with the same localization, at the same age and with the same complications, is more likely due to a constitutional peculiarity within the family. A non-specific congenital resistance of the body against tuberculosis is probably more important than a specific immunization which is acquired with a childhood infection. Different age-groups show a different type of reaction against tuberculosis; pulmonary tuberculosis of old people, for example, is characterized by an absence of propagation and by a marked tendency to fibrosis. Many so called degenerative stigmata have been singled out as indications of increased susceptibility to tuberculosis, such as polymastia, abnormally small mamillae, vascular and verrucous naevi, anomalies of the external ear, persistence of the interfrontal suture, abnormal length of the transverse processes of the lower cervical vertebrae, fluctuating tenth rib, absence of the right midlobe of the lung, cardiovascular hypoplasia, etc. Each one of these stigmata by itself is without significance. A constitutional analysis must take in account the entire body; a multiplicity of stigmata may indicate some abnormality of development. In some types of peculiar habitus it is difficult to decide whether it is the cause or the effect of tuberculous disease. The phthisical habitus has been interpreted as being particularly susceptible to tuberculosis, while other writers consider it as a consequence of tuberculous disease, and still others believe it to be merely a racial characteristic. The true asthenic habitus characterized by underdevelopment of musculature, poor development of fatty tissue, a heart which is too small in proportion to the lung, is probably more susceptible to tuberculosis than the arthritic habitus.—*Die konstitutionelle Disposition zur Tuberkulose, O. Satke, Wien. klin. Wchnschr., October 30, 1930, xliii, 1348.*—(*M. P.*)

Tuberculosis Contacts—It is generally felt that the results of contact examinations are not commensurate with the labor and time involved. Therefore an investigation was made in a locality with a population of three hundred and fifty thousand, in order to determine how many secondary cases of tuberculosis occurred up to the end of 1929, related to cases of pulmonary tuberculosis investigated and accepted by the tuberculosis officers during 1921 to 1924 inclusive. That is, there was a minimum period of five years and a maximum period of nine years for the possible discovery of secondary cases. The results show that known cases of pulmonary tuberculosis give rise to at least 15 per cent of secondary cases, in spite of modern antituberculosis measures, and that the average interval between the discovery of primary and secondary cases is three and one-half years. Based upon these observations, the following tentative conclusions are offered: *1:* The most profitable contact work is to be done among the families of patients with positive sputum, as these patients produce nearly all the secondary cases. *2:* It is most practical to limit attention to contacts on whom, for some reason or other, suspicion rests (suspects). *3:* Close contacts of patients whose sputum has contained tubercle bacilli should be kept under observation and reëxamined at intervals for at least four years. *4:* Relatively more attention should be paid to adult contacts who are not infrequently the source of infection. *5:* Welfare workers in large concerns can help materially in the

investigation of suspicious coughs or ill-health among employees. *6:* Wide dissemination of knowledge on health subjects, and growing familiarity of the public with medical examinations will facilitate examination of suitable contacts.—*The Examination of Tuberculosis Contacts, G. Jessel, Tubercle, August, 1930, xi, 493.*—(*M. E. P.*)

Tuberculosis Contacts.—The examination of individuals who have been in contact with tuberculous patients should be of value in determining the origin of infection and in detecting the earliest signs of disease. In order to consider contact examination at its best, there must be adequate time for complete investigation, sufficient clerical assistance and skiagrams of good quality. The power to prevent the spread of tuberculosis depends upon the ability to answer three questions: *1:* By whom was the patient infected? *2:* Whom has he infected? *3:* Whom may he infect? Little is known about primary infection and its relationship to later disease. The problem of childhood infection and its relation to adult disease remains to be solved, but meanwhile use of every modern method of investigation helps in the diagnosis of pulmonary tuberculosis in its early exudative stage, when collapse therapy can be used with fair prospect of success.—*Examination of Tuberculosis Contacts, W. B. Wood, Tubercle, August, 1930, xi, 489.*—(*M. E. P.*)

Pregnancy and Tuberculosis.—The question of tuberculosis and pregnancy has been much discussed, especially the influence of the puerperal state on the course of phthisis, which has been variously interpreted by different authors. Up to the end of the nineteenth century pregnancy was generally considered to have rather a favorable effect on the development of phthisis. Since then, following the works of Moriceau, Louis, and Dubreuilh, the opposite opinion has been maintained and the discussion continues. Recently in a long symposium held at the *Académie de Médecine* and the *Societé d'Obstetrique*, it was remarked that the results of the observations made were very contradictory. In the present report an attempt is made to classify the different clinical forms of tuberculosis. *Case 1:* In a girl of 26, concerns a torpid slightly active form, with bacillary sputum, in which neither pregnancy nor labor had any effect on the slow course of the disease, but in which the sanatorium cure exerted very favorable effects. *Case 2:* In a girl of 24, concerns an extensive pulmonary involvement, of a torpid kind, with reactivation following prolonged sanatorium treatment, manifested by slight febrile exacerbations which responded quickly to proper care, and by temporary increase in cough and sputum. *Case 3:* In a woman of 39, is one of a torpid type of tuberculosis not reactivated by pregnancy. *Cases 4 and 5:* In girls of 24 and 26, show a previously existing tuberculosis aggravated by the puerperal state, and resulting fatally. In the first case the initial manifestations of tuberculosis occurred six months after a first pregnancy and the patient meanwhile again became pregnant. The disease did not progress markedly until after her delivery. Unfortunately proper treatment for her tuberculosis was instituted quite late. *Cases 6 to 10:* Showed the first manifestations of the disease either at the beginning of, or during, pregnancy. Some, especially those with tuberculous family antecedents, no doubt were already affected with larval, occult forms of the disease. All of these patients, ranging in age from 19 to 32, died and the striking clinical feature is the rapid progression and gravity of their tuberculosis. *Case 11:* However, in a young woman of 25, shows that not all such are fatal. She had a unilateral right upper lobitis and later a basal corticopleuritis on the same side. Unilaterality of the lesions is a favorable factor, especially as it permits trial of artificial pneumothorax, which is often remarkably effective. Two such cases are presented in *Cases 12 to 13:* In women of 28 and 32, who also developed their first manifestations during pregnancy. There are now presented three observations in *Cases 15, 16, and 17:* In which the first manifestations of the disease occurred only after delivery, and to which occurrence Rist, Sergent and Küss have called attention. These were all quite young women. A point here arises as to how long a period following delivery may elapse before the development of the tuberculosis and the puerperal state still be considered a provocative factor? Sergent allows a year, Bernard six months, quite arbitrarily. As all three of the patients in question were still nursing their infants there seems little doubt that the puerperal state was a contributing factor. The youngest of the three developed bilateral fibrocaseous disease which resulted in death; the second recovered from a fibrocaseous right-upper-lobe involvement under artificial pneumothorax; the third had extensive bilateral lesions, predominating on the right side, and improved under prolonged sanatorium care. The observations thus far fall into the following groups from the standpoint of their tuberculosis: *1:* Patients presenting, prior to pregnancy, a torpid or feebly active pulmonary tuberculosis. Two such underwent pregnancy without harm. *2:* Patients presenting, prior to pregnancy,

extensive pulmonary involvement, with more tendency to caseation and febrile or subfebrile exacerbations responding to rest. In such cases gestation is likely to bring on a rapid development of the disease and the patient usually succumbs some time after delivery. *3:* Patients who experience during pregnancy, having been previously well, an attack of pulmonary tuberculosis. Its progress is often very rapid and usually fatal unless unilateral when it may be checked by collapse therapy. *4:* Patients who subsequent to delivery develop a tuberculosis which may vary in gravity from the curable to the fatal. In addition to the fibrocaseous forms there are others, generally more benign but which sometimes may lead to graver consequences. Among these the most common has been described by Bezançon under the name "tramitis," and by Dumarest as the "ganglion-interstitial" form of pulmonary tuberculosis, or further by Sergent as "perilobulitis." These forms are often unaffected by pregnancy (*Case 18*, age 25). In *Cases 19 and 20:* Ages 21 and 25, there occurred definite impairment of the general condition, accompanied by cough and loss of weight, which caused hygienic dietetic treatment to be adopted, with excellent results. In *Case 21:* The gangliohilar process extended to the perifissural (interlobar) region of the left side. There are also to be considered the predominantly fibrous forms which affect the general condition very little or may even go with a robust physique. These may be the site of congestive attacks which may manifest themselves by haemoptyses,—the haemoptoic fibrous forms. *Case 22* was such and remained unaffected by pregnancy. *Cases 23 to 25:* Also had haemoptyses at some time during pregnancy, without any evidence of progression or serious activity of the disease. There are also to be considered those cases of pleurisy associated with or preceding or following pregnancy. *Cases 26 to 31:* Were such and none showed any persistent tuberculous activity. Two of these pleurisies occurred in the interval between two closely following pregnancies. Thus, one must regard pregnancy as usually harmless to pleuritics, although *Case 32:* In a young woman of 25, later developed a parenchymatous involvement, responding to proper treatment. The last two cases have to do with pregnancy and glandular tuberculosis, in which no harmful effects were observed. *Children Born of Pregnant Tuberculous Women:* Here one should consider only viable children, removed at once from every tuberculous contact and properly nourished, in order that nutritional defects may not be laid at the door of tuberculosis. All fulfilling these conditions remained well and developed normally. Thus, while transplacental infection may be possible, it is actually exceptional, and this is further shown by negative cutireactions in those kept away from contacts. *Summary:* In a general way pregnancy and labor exert an unfavorable influence on tuberculosis and add an extra hazard to the prognosis. However, in actual practice aggravation is more or less to be feared according to the type of the disease. Some forms, especially the pleuritic, have a very good immediate prognosis; others, especially the rapidly progressive febrile forms, which do not respond to rest, are hopeless under the best conditions. Haemoptyses occurring in fibrous forms are less to be feared than in the ulcerating caseous. There is an intermediate group, the fibrocaseous, in some of which the fibrous tendency dominates, in others the caseating or ulcerating, and the prognosis varies accordingly. In arriving at a prognosis, many things must be considered, such as temperature, pulse general condition, extent of invasion of the lung, amount of sputum, etc. Cases showing occasional febrile exacerbations are most difficult to predict; some recover, others are incurable. These patients should be observed for some time, preferably at a sanatorium. Every pregnant tuberculous woman should be placed under the most favorable conditions for treatment as soon as possible. If this is done, many will support the pregnancy and come to term in a relatively satisfactory condition. If the disease is unilateral and shows evidence of activity, in addition to the hygienic rest treatment, one should institute collapse therapy (preferably artificial pneumothorax, or, if impossible, phrenicectomy) as soon as possible. The prognosis of extensive rapidly developing tuberculosis, with fever, is always bad and fatality may closely coincide with delivery. One is tempted in such cases to interrupt the pregnancy. But will this save the patient? Nothing is less certain, although Sergent and Küss have reported a small number of observations in which therapeutic abortion has had a favorable effect. In general, abortion is only justifiable if done early; after the third month its risks are just as great as are those of labor. Benign forms of tuberculosis, complicated by pregnancy, should be treated as are ordinarily more severe forms: prolonged sanatorium treatment until delivery, close supervision afterwards and more treatment if there is any impairment of the general condition. The children should be immediately isolated from any mother with bacilliferous sputum, even if only occasionally so. Vaccination of

the child with *BCG* is useful but should not cause neglect of the other precautions, especially in the early years. In the vast majority of cases these children, so treated, develop normally and remain free from appreciable tuberculosis.—*Trente-Quatre Observations de Tuberculose et Grossesse, J. Stiassnie, Rev. d. l. Tuberc., July, 1930, xi, 757.*—(*A. P.*)

Pregnancy and Tuberculosis.—The authors present the results of an analytical study of the obstetrical and gynecological histories from a group of 1000 women discharged from Trudeau Sanatorium. Of the group, 484 women answered the questionnaire in enough detail to make possible certain comparisons and observations, from which the following conclusions are deduced: *1:* Pregnancy has a definitely deleterious effect on tuberculous women. *2:* The more advanced the tuberculosis, the more deleterious the effect of pregnancy. *3:* The women who took sufficient time before getting pregnant after being "cured" (three years or more), and who obey all rules and regulations after leaving Trudeau, fared better than those who did not. *4:* Postpartum haemorrhage occurred in a very large proportion, amounting to 44 out of 317 cases, or 13 per cent. *5:* Menstrual disorders were very common among this group of tuberculous women, being reported by 47 per cent. *6:* Out of the 579 children born, 556 are alive, and 501 are healthy and well; 55 are below par, and only 9 of these have had tuberculosis in any form, or have been suspected. *7:* Education of the patient in the care of herself as regards tuberculosis as well as pregnancy is of the utmost importance.—*Pregnancy and Tuberculosis: Study of the Obstetric Histories of Four Hundred and Eighty-four Patients, H. B. Matthews and L. S. Bryant, J. Am. M. Ass., December 6, 1930, xcv, 1707.*—(*G. L. L.*)

Therapeutic Abortion in Tuberculosis.—This study is based on the observation of 1302 women who were referred to the chest clinic in order to decide whether abortion should be performed on account of tuberculosis. Two years after the decision had been made a check-up was done and it was possible to reëxamine 398 women, 254 of whom had been diagnosed as having tuberculosis. In diagnosing these patients Neumann's classification was used. With relatively few exceptions all women suffering from a frank phthisis were advised to be aborted. Women having the diagnosis of repeated pleurisies without pulmonary lesion, an inactive primary complex or a proliferating primary complex, dense fibrous tuberculosis or fibrous postpleuritic tuberculosis were generally advised not to be aborted. The check-up showed that the advice given was correct in practically all cases and it is concluded that Neumann's classification can well be used as a basis to decide whether therapeutic abortion is indicated or not.—*Ueber Schwangerschaftsunterbrechung wegen Lungentuberkulose, A. V. Frisch, Wien. klin. Wchnschr., November 20, 1930, xliii, 1441.*—(*M. P.*)

Iron Mining and Pulmonary Disease.—The inhalation of hematite leads to pulmonary fibrosis which is similar to that which follows the inhalation of white lead, but it is safe to say that the prolonged inhalation of dust from iron ore does not produce miners' phthisis. It does lead to bronchitis, a fine, diffuse fibrosis and shortness of breath, but it produces few other symptoms. Roentgenologically, the disease appears as a very fine, "grained" fibrosis, but is not like the so called "snowstorm" picture of silicosis, and the root shadows are exaggerated. The affection does not predispose to tuberculosis or other pulmonary disease.—*Dust Inhalation and Iron Ore Mining, E. L. Collis and K. W. Goodby, J. Industr. Hyg., September, 1930, xii, 266.*—(*H. S. W.*)

Infectiousness of Silicotic Tuberculosis.—It has been claimed that when tuberculosis complicates silicosis it is relatively benign as regards its spread to other members of the miner's household, but of this there is little direct proof. Of 24 cases (with positive sputum) no wife or widow had the disease; of 91 children in the families of these miners, 13 developed tuberculosis as compared to 8 out of 68 children in 24 families in which the father had tuberculosis without silicosis. The percentage of children under 14 at the time of the father's diagnosis in these miners' families and in comparable families of nonminers was 48 and 33.3 respectively. These few data are insufficient to base conclusions on, but they point the way to a similar study on more substantial numbers.—*The Infectivity of Silicotic Tuberculosis, P. Heffernan, J. Industr. Hyg., June, 1930, xii, 236.*—(*H. S. W.*)

Tuberculosis among Tobacco Workers.—The author studied the incidence of tuberculosis among 180 tobacco workers in the dispensary at Odessa who had been observed for more than 5 years. In 62.71 per cent there was no progression of the tuberculous process, while in 27.96 per cent there was a slow development and in 9.33 per cent a rapid progression of the disease.

The progression was associated in part with an epidemic of influenza and was partly due to starvation during the years 1921–1922. Added to this in a number of families was the unquestionably prolonged contact with open cases of tuberculosis. It is concluded that tuberculosis does not belong in the category of occupational diseases developing as the result of hazards in the tobacco industry.—*Zur Frage über Tuberkulose der Tabakarbeiter, M. L. Borschtschewsky, Zeitschr. f. Tuberk., 1930, lvi, 46.*—(*H. J. C.*)

BCG.—From November, 1924, to May, 1929, Sayé vaccinated 604 infants with *BCG.* However, in this study he includes only those done before April, 1928, for whom there is therefore a record of from one to four and one-half years duration. These total 346, of whom 10 per cent were vaccinated in lying-in clinics, the rest at home by visiting nurses or a physician. Most of them, 332, were vaccinated by the oral route, and only 14 subcutaneously. In this study a control group is compared with the foregoing, consisting of 343 nonvaccinated children, aged from birth to four years, mostly belonging to families followed by the dispensary. The vaccinated children were examined by Sayé or his coworkers at least twice yearly, while the control group were examined during the last six months and in doubtful cases further investigations were carried out. In both groups the intracutaneous reaction was practised, up to 1927 with 0.2 cc. of Old Tuberculin in a 1–5000 dilution, and since then with 0.1 cc. of a 1–1000 dilution, or 0.1 mgm. tuberculin. In certain cases the Pirquet method was used. In many cases examination was supplemented by fluoroscopy and roentgenography. The economic and nutritional conditions of the two groups were similar. The vaccinated children living in a favorable environment were compensated for by a portion of the control group living under good hygienic conditions, of a private clientele. They were quite few, the proportion born and brought up under unhealthy conditions being 76 per cent, and under very unhealthy conditions 52 per cent. The fact that most of the infants were breast-fed is of little significance as they soon received nourishment from other sources, often quite inappropriate to their needs. The vaccinated children have been divided into two groups: *A:* Those in bacilliferous contact. *B:* Those without known tuberculosis in the family. The control group were similarly divided into *C* and *D* groups. Further, groups A and C (bacilliferous contacts) have been subdivided into **subgroups** *M* (massive contagion) and *P* (paucibacillary contagion). *Group M* includes: *1:* Children born of mothers suffering from serious tuberculosis with activity during pregnancy and who were not separated before, or sometimes after, vaccination. *2:* Children of a father seriously diseased and in intimate contact with him either from birth or later. *3:* Children who lived in contact with a very contagious patient,—not always a relative. *4:* Children exposed to multiple sources of serious contamination. The clinical forms of lesion found in children of the above (massive contagion) group were the exudative-pneumonia, bronchopneumonia, caseous pleuropneumonia, active fibrocaseous forms, ulcerative fibrous forms, chronic miliary disease ("granulie"), etc. *Group P (paucibacillary)*: Includes children who have lived in contact with patients (relatives or others) having (1) torpid fibrous or fibrocaseous tuberculosis, with intermittent or very slight bacillary elimination; (2) benign septicaemic forms, lymphatic, bone or cutaneous manifestations; (3) processes, possibly at first malignant, treated with good results by hygienic methods, collapse therapy or chemotherapy, with inconstant or no elimination of bacilli. As to results in the children, the following groups have been distinguished: (1) children dead of a tuberculous affection whose nature was controlled by necropsy or by clinical symptoms plus complementary examinations; (2) children dead of diseases probably tuberculous but for whom such confirmation was not obtainable; (3) children dead of manifestly nontuberculous diseases; (4) children afflicted with nontuberculous diseases; (5) healthy children, including (a) those of normal weight or slightly below, who have had benign affections of no serious consequence, and are designated +; (b) those of normal weight or slightly above who have had only slight indispositions, designated ++; and (c) those of normal or supernormal weight who have never been sick, designated +++. In the "tuberculous morbidity" group are included (a) grave tuberculous processes;—pneumonic gangliopulmonary forms and generalized tuberculosis; (b) less grave tuberculous processes;—diffuse primary infiltrations, curable splenopneumonias, or "epituberculous" infiltrations, Ranke's secondary phases in the initial stage, discrete bacillaemias, complicated tracheobronchial adenopathy, exudative phenomena in lung or pleura, massive tracheobronchial adenopathy, etc.; (c) benign tuberculous processes;—discrete tracheobronchial adenopathies, mediastinofissural lesions or retrogressive mediastinopulmonary lesions, or retrogressive primary lesions. It may be seen from table I that 36 per cent of the

vaccinated children had massive contagion, as compared with 66.5 per cent of the controls, and that in addition there was a group of 91 vaccinated without known contact, and 84 unvaccinated. Table II shows the number of each group vaccinated in the different age-periods (years after birth). Table III shows the 323 controls separated into groups according to age of exposure to contagion and its type (massive, paucibacillary, none known). *Results:* Nine premature children were vaccinated, weighing from 1800 to 2600 gm., and 11 hereditary syphilitics. No untoward incidents or disturbance of nutrition occurred. *"Allergic" Reactions:* With positive contact children, the proportion of positive tuberculin reactions increases each year and is highest in those exposed to massive contagion. But those without known contact do not show as low a proportion of reactors as might be expected, a little less than one-third reacting. The difference between the "massive contagion" group and the others is most striking for the first year. *Roentgenographic Observations:* These are tabulated according to a numerical symbol system, which is explained. *1: Vaccinated Children:* The following roentgenographic images have been seen: fine nodules, localized shadows, and a combination. They have been most frequent on the right side and in the lower two-thirds of the field. Only exceptionally have the attributes of exudative phenomena been noted: one mediastinopulmonary, two mediastinofissural, one pleurisy and one localized infiltration. In one case without known contact there was a picture of advanced retrogression of a primary lesion. Among the vaccinated children under one year and in a paucibacillary environment, the proportion of those with nodular hilocentral and hilobronchial images and shadows was about the same. In the second year children more nodules were seen, but in the third and fourth fewer. Among those exposed to massive contagion the proportion was about the same for the first two years. In the third year the presence of associated or combined lesions was more common. In children without known contact during the first year only isolated nodules or discrete shadows were noted and some rare hilar shadows. In the fourth associated lesions began to appear. Groups *M* and *P* show interesting analogies, also noteworthy differences. Among the analogies may be mentioned the frequent mediastinal localization of lesions, their limited extent and their cycle of development. Among the differences are the greater number of shadows in cases of massive contagion from the ages of six months to three years. In group *M* exudative periglandular phenomena appear earlier and are more marked. Among a total of 204 children X-rayed, 42 per cent reacted to tuberculin. The presence of lesions usually coincided with a positive tuberculin reaction. Nodular lesions in general tend to appear most frequently during the third and fourth years. A fair proportion of nodular images (58 per cent) was noted in subjects not reacting to tuberculin. Primary exudative types of lesion were noted in 12 per cent of unvaccinated cases exposed to massive contagion and 4 per cent exposed to paucibacillary contagion. Grave types of lesions in general were noted in 43.9 per cent of the unvaccinated exposed to massive contagion and 20 per cent exposed to paucibacillary contagion. On the other hand, in the vaccinated exposed to massive contagion the figure was only 7.8 per cent. It is concluded that children vaccinated and exposed to massive contagion show, in number, character, and type, much more benign processes than do a similar unvaccinated group, of the same age and degree of exposure. In a paucibacillary environment vaccinated children seem not susceptible to virulent infection and never show more than discrete and benign lesions. Children without known contact, vaccinated, rarely show pathological changes, while the unvaccinated often do. *Morbidity: 1: Nontuberculous Diseases:* These were noted in 14 of the vaccinated children. Most common were diseases of the respiratory and digestive tracts, usually benign; whooping-cough, measles, grippe and tonsillitis; 6 cases of various cutaneous affections; a few of rachitis and bronchiectasis, the latter condition being noted in children with hereditary syphilis. In general, nontuberculous diseases were more frequent and serious in the unvaccinated group. *2: Tuberculous Diseases:* Six vaccinated children exposed to massive contagion from birth or shortly after developed tuberculous processes. All but one reacted positively to tuberculin and all developed clinical manifestations within the first two years. In one case the positive tuberculin reaction was delayed five months. One of these cases was an attenuated tuberculous pneumonia, together with spina ventosa, two were slight lesions and four others confined to the tracheobronchial glands. In the control groups exposed to massive contagion, on the other hand, the frequency of serious processes, those of medium gravity, and benign, increases progressively with age and is in general rather high, the total reaching 88.5 per cent at the end of the fourth year, of which 7.7 per cent were very serious, 34.6 per cent moderately so. Seven vaccinated children exposed to paucibacillary contagion developed clini-

cally tuberculous manifestations, all during the first two years. Four of these reacted positively to tuberculin but in one allergy was intermittent and in another developed quite late. There were noted one process of moderate severity, one diffuse exudative form associated with primary infection which developed favorably, and the others were benign processes, discrete tracheobronchial adenopathies, which developed favorably. Among unvaccinated children exposed to paucibacillary contagion there were three times as many tuberculous manifestations developing in the first two years, and many others during the third and fourth years, so that a total of 96.4 per cent were affected. The proportion of benign lesions, however, is from two to three times that of the more severe. In the vaccinated children without known contagion, only one child in its first year suffered from chronic digestive disturbances and during its fourth year showed signs of retrogression of a primary lesion. Of the unvaccinated without known contagion, 24.2 per cent of those passing the fourth year showed evidence of a tuberculous process, rarely very severe. It may be concluded that: *1:* Among the vaccinated there were no cases of grave tuberculosis. *2:* Benign and moderately severe lesions were noted only during the first two years, while in the unvaccinated they were frequent up to and including the fourth year. *3:* In the vaccinated children even benign processes are uncommon, which is not the case with the unvaccinated. *Mortality: A: Children Exposed to Massive Contagion:* Concerning the vaccinated the figures show a mortality only in the first two years, and that is slight, especially for the second year. The 6 children who died have been in contact since birth, five with the mother and one with the father, without any precautions being taken. There were also 7 children who died of diseases "probably tuberculous" in nature. In 4 cases there was maternal contamination, in 2 multiple, and in 1 collateral. The stated diagnoses were tuberculotoxic gastroenteritis, progressive denutrition, bronchopneumonia, septicaemia. There were 13 children who died of nontuberculous diseases, 10 during the first year. These were acute and chronic gastroenteritis, 8; athrepsia, measles, bronchopneumonia, typhoid fever, hereditary syphilis. Concerning the unvaccinated, one-third showed localized forms and two-thirds generalized. The highest mortality figures were in the first year, but were considerable also in the second and third years. On the other hand, the nontuberculous mortality was not high, showing that contamination and not lack of general resistance was at fault. Comparison between these two groups shows that (1) deaths in the vaccinated from tuberculosis occurred only during the first two years, and (2) for the first year the tuberculosis mortality in the vaccinated was one-third of that in the others, and the mortality from "probable tuberculosis" much lower. Moreover, the general mortality was low in the vaccinated group, especially during the third year. *B: Children Exposed to Paucibacillary Contagion:* In the vaccinated group, a mortality "of probably tuberculous" cause occurred only in the first year and that was low. Also, the nontuberculous mortality was low (bronchopneumonia, acute gastroenteritis, malignant tonsillitis, rachitis, epidemic meningitis, etc.). Of 21 who died of all causes, 17 were contaminated by the mother. In the unvaccinated group, deaths decreased from the first year on. There were 8 generalized and 2 localized forms of tuberculosis, also 7 deaths from other causes. *C: Children Not Exposed to Known Contagion:* There were 9 deaths under two years in the vaccinated, one probably due to tuberculosis. This is the only group in which the unvaccinated showed a lower mortality and it was a small one. *Summary of Mortality Figures for Vaccinated and Unvaccinated Children:* For the first year, those in contact with massive contagion, the tuberculous mortality was 5.4 per cent for 92 vaccinated, 14.5 per cent for 159 unvaccinated; adding those dead from "probably tuberculous" causes, we have 12 per cent for the vaccinated and 23.3 per cent for the unvaccinated. For the second year, the known tuberculous mortality was 1.6 per cent for 61 vaccinated, 5.4 per cent for 93 unvaccinated; adding deaths from "probable tuberculosis," we have 3.3 per cent against 10.8 per cent. Considering the "paucibacillary contact" group, the figures for the first year show only 1.22 per cent mortality (known and probable tuberculosis) for 163 vaccinated, against 12.5 per cent for 80 unvaccinated, and for the second year no tuberculous mortality for 91 vaccinated and 3.63 per cent for 55 unvaccinated. Thus, during the first year vaccinated children living in an environment of massive contagion showed half the tuberculosis mortality of the other group, as well as a slightly lower general mortality. The paucibacillary contacts who had been vaccinated showed a very low mortality from known and probable tuberculosis, during the first year, one-tenth that of the unvaccinated. Thus, vaccination seems to be most effective in preventing clinical forms of infection from developing when there is paucibacillary contact during the first year, usually maternal. If all the groups based on degree of contact are combined, we find that of 255 vaccinated

children the first year mortality from definite and probable tuberculosis was 5 per cent, against 19.7 per cent for 239 unvaccinated; the mortality from other causes 9 per cent, against 6.3 per cent; of 152 vaccinated children the second year mortality from definite and probable tuberculosis was 1.3 per cent, against 8.1 per cent for 148 unvaccinated; while the mortality from other causes was 5.3 per cent in the vaccinated, 2.7 per cent in the unvaccinated. After the second year there was but a single death (nontuberculous cause) in 80 vaccinated children, while there was a 6.6 per cent mortality in the third year among the unvaccinated, mostly from tuberculosis. (*N. B.*—Here it appears from the tables that the term "general mortality" is inclusive of tuberculosis mortality.) These results are affirmed to show a favorable effect of vaccination on both the tuberculosis and the general mortality. *Infants Vaccinated Subcutaneously:* There were 14 such, 2 in an environment of massive contagion, 11 in a paucibacillary one and 1 without any known contagion. One child was vaccinated at birth, the others, at ages ranging from 1 to 18 months. In 3 cases a dose of 1 mgm. was used, in 5 one of 0.5 mgm., and in 6 only 0.25 mgm. The three given the largest dose and the five given 0.5 mgm. all developed characteristic abscesses, but only one such was observed using 0.25 mgm. All became allergic to tuberculin. Two children died, one of gastroenteritis at eight months and one was a hereditary syphilitic with bronchiectasis. The others are free from ill health and their condition is characterized as 1+, 5++ and 6+++. *Revaccinations:* A group of 97 children were revaccinated: 67 from twelve to eighteen months, 16 from eighteen to twenty-four months, 8 from twenty-four to thirty months, 6 from thirty to thirty-six months. Twenty of these children belonged to the group "without known contagion," 50 to Group *P* and 27 to Group *M*. Nothing untoward followed the revaccinations. *Health of Vaccinated Children:* Of 92 observations in children exposed to massive contagion, 56, or 60.9 per cent, were healthy; of 163 paucibacillary contacts, 129, or 79.1 per cent, and of 91 without known contagion, 73, or 80.2 per cent. In 92 per cent of cases the vaccinated children have been well developed. There are scarcely adequate figures for the control group, as this has only been well followed for the last six months and only a single examination made of each child. However, of 158 exposed to massive contagion, only 15 per cent were apparently healthy, and of 81 paucibacillary contacts, only 4, or 4.9 per cent. In the vaccinated child, as can be affirmed from tuberculin tests and roentgenographic pictures, the "ante-allergic phase" in a contaminated environment is more prolonged. If the allergy due to virulent bacilli is expressed by the neoformation of tuberculous tissue, and if vaccination renders a child less susceptible to such infection, the proof should be at hand. In fact, even in children born under the most unfavorable conditions, in whom virulent infection must be practically contemporaneous with vaccination, the number of cases of tuberculosis is less than among the controls. The topography and character of the lesions differ. The mediastinal lesion, which in unvaccinated children frequently extends into the parenchyma or interlobar fissures, in vaccinated children is more restricted and localized and much periglandular pathological change is uncommon or slight. This difference must signify a strengthening of the defenses of the organism so that the virus is localized in the lymphatic system. If such immunity, or relative immunity, can be conferred on a wide scale,—and it is not necessarily accompanied by an allergic state,—it may last several years and help check the activation of small tuberculous foci following acute infectious diseases of childhood. With further precautions and supervision still better results ought to be obtainable, even though those at hand are quite remarkable. *Conclusions:* From November, 1924, to May, 1928, there were vaccinated with *BCG* 368 children, on 346 of whom there are adequate records. All but 14 were vaccinated by the oral or ingestion method. The results are compared with those among 323 unvaccinated children from birth to 5 years of age who lived under practically the same conditions. Those exposed to massive contagion were somewhat more numerous among the controls but each group has been separated. The vaccinated children in general became allergic rather later than the unvaccinated and those exposed to massive contagion showed roentgenographically more benign types of processes. Both morbidity and mortality records favor the vaccinated. Making allowance for the nature of the contagion, the results for the first year show a general mortality of 14.1 per cent for the vaccinated and 25.9 per cent for the unvaccinated. The tuberculosis mortality figures vary still more: 5.1 per cent for the vaccinated, 19.7 per cent for the unvaccinated. For the second year, the figures show a general mortality of 6.6 per cent for the vaccinated, 10.8 per cent for the controls, and a tuberculosis mortality of 1.3 per cent for the vaccinated against 8.1 per cent for the controls. For the third year there is no mortality for the vaccinated against 6.6

per cent for the controls. The effectiveness of this method seems self-evident. If the use of *BCG* can be combined with isolation for two months afterward of the child, the results should be much better. It would seem also that most of the tuberculous processes developing in adults from antecedent virulent infection should also be prevented. A considerable number of statistical tables and several roentgenographic reproductions are included.—*Sur la vaccination antituberculeuse avec le BCG Séries d'observations de 1924 à 1928, .L. Sayé, Rev. d. l. Tuberc., December, 1929, x, 781.*—(*A. P.*)

BCG.—Animal experiments have shown that the parenteral administration of *BCG* is capable of producing an increased resistance against a virulent infection. But a marked effect is obtainable only when large doses are given, and only by parenteral administration. Experiments on animals would indicate that the enteric administration of *BCG* affords less protection than Koch's and Behring's bovovaccination; and these procedures have failed in their practical application. The individual variations in the natural resistance of rabbits against tuberculous infections are greater than the increase in resistance which can be brought about by *BCG* vaccination. The resistance evidenced by the chronicity of most tuberculous reinfections is usually explained as being caused by the primary infection; it is suggested that the importance of this immunizing action of the primary infection is overrated. Under the assumption of marked individual variations in the resistance against tuberculosis, it is only the naturally resistant individual which survives a primary infection. A second infection is chronic and localized as a rule (indicating resistance) not because the first infection conferred immunity, but because the individual is constitutionally resistant, as proved by the fact that he survived the primary infection. A healed primary focus is then not the cause but only an evidence of high resistance. The changes in the specific reactivity of the body produced by the first infection are markedly influenced by the constitution of the respective individual. They are most marked in the most susceptible animal, the guinea pig. This explains the fact why even so mild an infection as is produced by *BCG* yields demonstrable effects in guinea pigs, but much less so in more resistant animals. By an artificial infection a certain increase in resistance can be produced, but this specific immunity is dependent primarily on the constitutional susceptibility: the susceptible individual acquires a certain protection against a second infection only by tuberculous disease, the resistant individual survives the primary infection on account of his natural immunity, the primary infection, however, being not the cause of his resistance. It remains questionable whether a safe and efficient vaccination against tuberculosis is possible. As far as Calmette's method is concerned, its effectiveness has not been proved.—*Immunität und Schutzimpfung bei Tuberkulose, K. Lydtin, Klin. Wchnschr., December 6, 1930, ix, 2281.*—(*M. P.*)

BCG.—*BCG* does not produce progressive tuberculosis in experimental animals. Examinations of Petroff's "dissociated" cultures of *BCG* has proved that both rough and smooth colonies are virulent and are of human type rather than the original bovine type. Animals inoculated with *BCG* are being proved to have acquired a limited immunity. Calves and young lambs which were fed with cultures of *BCG* received much smaller protection than similar animals received when the culture was inoculated. The protection which guinea pigs acquire from *BCG* retards the progress of disease while in sheep and calves complete protection against a fatal dose may be obtained. Calmette's culture has the advantage that it may be repeatedly applied. Experience with *BCG* in human beings as well as in animals shows that an absolute protection cannot be obtained, for as yet a natural infection with virulent bovine tubercle bacilli does not safely protect against a later infection with human bacilli. The course of tuberculosis is dependent mainly upon the natural constitutional defensive mechanism of the individual, rather than upon a specific, acquired immunity. It may be expected that such children as possess a certain amount of "defensive bodies" may, by vaccination, more easily overcome a tuberculous infection. It is difficult to observe a sufficient number of vaccinated and nonvaccinated individuals over a number of years when they have as chronic a disease as is tuberculosis. It is particularly difficult to observe people that are equally exposed to tuberculous infection and that live under similar hygienic surroundings for a long time. The results from *BCG* vaccine are probably the best that we may hope to obtain from a protective vaccination. *BCG* should be used to a greater extent in children particularly exposed to infection.—*Die Tuberkuloseschutzimpfung mit BCG, F. Neufeld, Deutsche med. Wchnschr., September 19, 1930, lvi, 1599.*—(*H. S. W.*)

BCG.—Since 1927, an attempt has been made at the Hospital for Sick Children, Göteborg, Sweden, to reduce the mortality

of infants exposed to tuberculosis, by the use of *BCG*. Instead of the oral administration according to Calmette, intracutaneous injections have been employed, because "tuberculin-allergy" occurs earlier and with greater certainty with this method. Such an allergic reaction is considered evidence of immunity. Until the appearance of such a reaction, the children have been protected from all virulent tuberculous infection. During the past three years, 106 children have been thus vaccinated, all from families with open bacillary infection. Of these, 44 have not yet been in contact with a tuberculous person after vaccination, and so are of no importance in the present study. (Two have died of acute pneumonia; all the other 42 are well.) The remaining 62 children have lived in contact with consumptives for varying numbers of months, the majority for two to three years. During the past two months, these 62 have been examined clinically and radiologically. None presented clinically demonstrable tuberculous disease; and only two gave radiographic evidence of hilum involvement. For the result obtained, it seems proper to give the vaccine some credit. But the fact that no infant was exposed to tuberculosis during the first six weeks of life (most of them being free from contact during the first six months) must also be taken into account. Again, all infants were isolated until they had reacted to the tuberculin injection, namely, from three to twenty-one weeks. The use of vaccination makes it easier to convince parents of the necessity for isolation.—*De rôle de la vaccination anti-tuberculeuse par le B. C. G. dans la lutte contre la tuberculose infantile, A. Wallgren, Nourrisson, January, 1931, xix, 53.*—(*P. J. W.*)

BCG in Amsterdam.—During the course of 4 years 264 newborn infants were given *BCG* orally. Only exposed sucklings were treated, at first limited to family contacts and later to those of extrafamily hazards. In no case was even the slightest harm from treatment noted. One child treated showed swollen mesenteric lymph nodes containing tubercle bacilli on section, indicating the permeability of the intestinal mucosa for *BCG*. The tuberculosis mortality among the treated children was lower than for those not treated. There is a decided resistance to infection in the *BCG*-inoculated children.—*Die Resultate der BCG-Imfungen in Amsterdam. M. R. H. van den Berg, Zeitschr. f. Tuberk., 1930, lv, 401.*—(*H. J. C.*)

BCG in Roumania.—During the years 1926, 1927 and 1928, 17,535 children were vaccinated with *BCG*. Of this number, 1005 lived in contact with active tuberculosis and were never isolated. No ill effects were observed. In areas where large numbers of children were vaccinated, the general mortality rate was diminished by one half. *BCG* confers an undoubted immunity and raises the resistance against the disease. Vaccination should not be limited entirely to infants born of tuberculous parentage, or those living in contact with the disease. All infants can be rendered immune by prompt vaccination soon after birth; isolation should be practised as much as possible even after vaccination.—*Resultats de trois années de vaccinations antituberculeuses par le BCG en Roumanie, M. Cantacuzene, meeting Acad. de Méd., November 5, 1929, reported in Progrès Méd., November 23, 1929, no. 48, 2064.*—(*U. E. Z.*)

BCG in Lübeck.—The Ministry of the Interior issues the following communication regarding the deaths of infants in Lübeck: The epidemiological course of the disease has shown periodical fluctuations which indicate that the vaccines, prepared and administered at different periods, were of a different virulence. The *BCG* culture as received from the Pasteur Institute proved to be pure and without virulence for guinea pigs. Guinea pigs inoculated with tissues from the dead infants developed progressive tuberculosis. Cultures from such tissues showed a high degree of virulence for guinea pigs, but were less virulent to rabbits, therefore corresponding to cultures of human tubercle bacilli. The investigation is still in progress.—*Das Reichsministerium des Innern zu der Katastrophe in Lübeck, Deutsche med. Wchnschr., September 19, 1930, lvi, 1625.*—(*H. S. W.*)

BCG in Lübeck.—In animal experimentation it has been observed that *BCG* cultures, when introduced intraperitoneally, lead to tuberculous inflammatory changes in the omentum, the intestinal lymph nodes and, occasionally, also in the spleen and liver. A question is raised as to the possibility that similar changes may occur in the intestinal tract following oral admission of *BCG* in infants. If this is so, may not such reacting areas form a point of lowered resistance for the deposition and growth of human tubercle bacilli of either exogenous or endogenous origin. In autopsies a search for human tubercle bacilli should be made in the intestinal tract and its glandular system. If human tubercle bacilli could be demonstrated, other theories may be advanced as to the change of the *BCG* strain into virulent forms in the cultures or in the vaccinated individual.—*Bemerkungen zu vorstehendem Artikel (fol-*

lowing M. Kaplan, Deutsche med. Wchnschr., September 12, 1930, 1563), E. Friedberger, Deutsche med. Wchnschr., September 12, 1930, lvi, 1563.—(H. S. W.)

BCG in Lübeck.—Thus far, approximately 50 children in Lübeck have died of tuberculosis following vaccination with *BCG*. What are the principal factors involved? In 1908, Calmette recovered a highly virulent strain of bovine tubercle bacillus from the milk of a tuberculous cow. This strain up to 1928 had been transferred 347 times on potato-bile medium and had entirely lost its virulence for human beings. In 1921, he began inoculating it into human beings. Yet, frequently, experiments have shown that *BCG* is not entirely innocuous for animals. This might be true also in human beings in whom the bacillus may undergo a gradual transformation into a virulent form. This transformation is probable in cases of sporadic endemics which have been reported, but not in the cases at Lübeck. Another possibility may be seen in the fact that bacilli by their removal from this particular medium may become virulent again. This happens with certain other bacteria. (May dissociation be responsible?) The apparent avirulence of *BCG* may come from the fact that the majority of the colonies are of the so called "R" form, from which occasional "S" (virulent) forms are dissociated. This may explain the virulence of the strain in Lübeck, because cultures have been grown on egg medium which are favorable for the development of the "S" forms. Further inoculation of *BCG* should be prohibited until the strain is studied more in animals.—*Beträchtungen über die Misserfolge der Calmette-Impfung mit BCG in Lübeck, E. Friedberger, Deutsche med. Wchnschr,. August 1, 1930, lvi, 1300.—(H. S. W.)*

BCG in Lübeck.—A definite decision as to the deaths of infants in Lübeck following vaccination with the Calmette vaccine has not been reached and further investigation will probably be under way for several weeks. Thus far it appears that the original Calmette culture received from the Pasteur Institute was probably unobjectionable, but in Lübeck it was recultured for 8 months on different culture media and was then used for vaccination without preliminary animal inoculation test as to virulence.—*Zur Frage der BCG-Schutzimpfungen in Lübeck, M. Kaplan, Deutsche med. Wchnschr., September 12, 1930, lvi, 1563.—(H. S. W.)*

Experimental Immunization with BCG.—Two *Macacus rhesus* monkeys, given 50 mgm. of *BCG* subcutaneously, remained free from tuberculosis 14 months after the intracutaneous inoculation of 0.1 mgm. of virulent human tubercle bacilli, while two control animals, dying of intercurrent infections in 57 and 60 days, revealed a generalized tuberculosis. An additional 10 monkeys experienced an increase of 18.6 days' duration of life over those not given *BCG*, but all the animals showed a caseous tuberculosis.—*Studien über Tuberkulose. V. Versuche, durch Erstimpfung mit BCG.—Impfstoff den Ablauf einer Superinfektionstuberkulose zu beeinflussen, A. Nohlen, Beitr. z. Klin. d. Tuberk., 1930, lxxiii, 525.—(H. J. C.)*

Mutations and Pathogenicity of BCG.—The pathogenic properties of two strains of *BCG* were investigated. Deep bouillon subcultures of the first strain (I) produced generalized tuberculosis in all of 28 guinea pigs which were inoculated intraperitoneally with doses of from 0.1 to 20 mgm., and produced severe progressive tuberculous lesions in all of 12 rabbits inoculated intravenously with doses of from 5 to 20 mgm. Twenty-two of 23 guinea pigs infected either directly with tuberculous material from these animals, or with cultures from the tuberculous material, developed generalized tuberculosis. The second strain, *BCG* 359, proved less virulent. Deep bouillon subcultures were tested on 56 guinea pigs, 12 of them receiving doses of 10 mgm. intraperitoneally. Of these 12, three which were killed and 2 which died had definite progressive tuberculous lesions. Before final conclusions as to the pathogenicity of tubercle bacilli can be drawn it is very important that the animals should be kept under observation for a period, not of months but of years. Agreement is expressed with Petroff and Watson that in the great majority of experiments on the pathogenicity of *BCG*, the animals have been killed too soon after inoculation. It is likely that part, at least, of the difference in virulence noted above is inherent in the strain. Thus, Petroff and Steenken found that culture *BCG* 359 was more difficult to dissociate into "R" and "S" colonies than the three cultures previously obtained. In seeking for an explanation for the development of a relatively high virulence of *BCG* in these experiments, it is considered possible that the cultural methods employed favored the development of organisms analogous to the "S" type of Petroff, and partially suppressed the growth of the "R" type. The use of deep bouillon cultures of *BCG* resulted from the observation in the course of some experiments on tuberculosis that cultures grown in the depth of the medium were occasionally, but not regularly, very much more virulent than cultures grown on solid media or on

the surface of liquid media. The present knowledge of the biology of *B. tuberculosis* is too rudimentary to enable one to predict with any degree of certainty the stability or variability of any property such as pathogenicity, and therefore the use of living cultures for immunization may be associated with some degree of danger. Photographs and full tables of the experiments accompany the article.—*Mutation and Pathogenicity Experiments with BCG, G. Dreyer and R. L. Vollum, Lancet, January 3, 1931, ccxx, 10.*—(*E. H. K.*)

Milk Control.—Numerous diseases may be propagated by milk, of which the most important are tuberculosis, paratyphoid fever and dysentery. Pasteurization destroys most of the pathogenic bacteria of these diseases, but the streptococcus and the tubercle bacillus sometimes survive it, although they are greatly reduced in number. Of 34 guinea pigs inoculated with pasteurized milk having a large artificial concentration of tubercle bacilli, 2 developed tuberculosis. In the larger cities of the United States, 95 per cent of the milk is now pasteurized. Pasteurization should be universally applied. In Germany pasteurization is much less universal than in the United States, and infection of human beings with bovine tuberculosis is high (6 to 8 per cent). In New York the mortality of infants from tuberculosis fell from 609 in 1898 to 93 in 1923. This decrease is obviously due, in part, to improvement in general hygienic measures, but it is a remarkable result and occurred during an extension of pasteurization.—*Gesundheitswesen u. Krankenfürsorge, Trendtel, Deutsche med. Wchnschr., July 18, 1930, lvi, 1221.*—(*H. S. W.*)

Pasteurization of Milk.—The systematic pasteurization of ordinary market milk intended for consumption in large urban areas is, according to the author, unavoidable under conditions where milk is collected and mixed from widely scattered and varied sources, and not under such scrupulous control as to eliminate the risk of chance infections. It is of real protective value against bovine tuberculosis.—*The Place of Pasteurization in a Scheme of Milk Distribution, A. S. M. MacGregor, Brit. M. J., September 20, 1930, no. 3637, 463.*— (*M. E. P.*)

Tuberculin in Prevention of Tuberculosis.—There is a general agreement that the subcutaneous tuberculin test is a reliable indication of tuberculous infection. Specific immunization may be regarded as a prime factor in curative and preventive treatment. To ascertain the curative power of tuberculin, a patient with a positive tuberculin reaction, was given fifty inoculations with a bacillary emulsion. After this treatment, the tuberculin test was negative. This is presented as a probable example of the curative efficacy of tuberculin treatment.—*Prevention of Tuberculosis by means of Tuberculin, R. Carswell, Brit. M. J., October 11, 1930, no. 3640, 597.*—(*M. E. P.*)

Pathology of Tuberculosis.—This is a brief review of some of the newer problems in pathology and bacteriology of tuberculosis. There is much discussion on the question whether nonacid-fast forms of the tubercle bacillus exist. Much's granules are interpreted by some authors as a certain developmental stage in the life cycle of the tubercle bacillus, while others believe that they are disintegration products of no practical significance. The question of the filterable, nonvisible virus is not settled. While Calmette is convinced of its existence, it is denied by other workers. Histological studies have established the fact that the pathogenic action of tubercle bacilli may cause either exudative or proliferative processes which are usually found combined. Either one of the two lesions is regularly preceded by a primary injury to the tissue. But it is not correct that productive lesions are always preceded by exudative processes as has been claimed by some authors. Whether productive or exudative processes dominate depends on the severity of the infection and on the resistance of the host. Postmortem studies and tuberculin tests have shown that the majority of adults have undergone a tuberculous infection, usually in childhood. The most frequent mode of infection is that by inhalation. Intrauterine infection is rare, and there is no proof that a true germinal infection occurs. The anatomical proof for the portal of entry is given by the tuberculous primary complex, which with sufficient care can be demonstrated in almost every case when it exists in the lung. The primary complex may develop immediately into progressive disease, but as a rule it heals and later disease is caused by a superinfection. The primary infection occurs most frequently in the nonapical parts of the lung while later infections are most frequently found in the apices. In contradistinction to this well-established concept, recent writers have claimed that reinfection foci are most frequently localized below the clavicle and that they are acute exudative processes. The difference between the old and new teaching has been mitigated because the representatives of the old teaching have admitted that the so called early infiltration plays an important rôle in the development of tubercu-

losis, while the representatives of the new teaching have conceded that apical foci are not always as harmless as first represented. The relation of apical foci to early infiltrations and the pathologico-anatomical structure of the early infiltrations are still uncertain.—*Ueber einige neuere Probleme aus der pathologischen Anatomie der Tuberkulose, C. Sternberg, Wien. klin. Wchnschr., September 25, 1930, xliii, 1207.*—(*M. P.*)

Recent Laboratory Investigations in Tuberculosis.—Since the discovery of the art of percussion by Auenbrugger and Corvisart's emphasis on physical diagnosis as the keystone of medical practice, followed by Laennec, who clarified scientifically the physical diagnosis of chest lesions, there has accumulated a rich heritage of signs and indications, which perhaps reached their fullest interpretation in the genius of Sir William Osler. However, with the advent of more or less routine pathological studies, it soon became evident to clinicians that, even with the closest observations with the unaided senses, there were cases which at necropsy revealed quite unforeseen lesions. The later development of the X-ray and its application have reduced materially the number of cases presenting unsolved problems. Yet, with the aid both of careful physical examination and X-ray films, the honest clinician will probably admit that there remain cases in which tuberculosis is suspected but the diagnosis and prognosis are obscure. Certain additional criteria are now being acquired through laboratory investigations which promise to further promote our understanding of certain phases of this subtle disease. *Peripheral Blood Count:* Attention has recently been focussed on a fine differentiation within the mononuclear group of cells and from the studies of Sabin and coworkers on experimental tuberculosis is coming a new appreciation of the value of the blood count in the diagnosis and prognosis of the disease. Supravital staining technique has contributed materially. The normal monocyte is a cell both of connective tissues and blood and the unit from which the epithelioid and Langhans' giant cell derive. The lymphocyte, represented in the blood and lymphoid tissues, makes up the capsule of small round cells which characteristically surround a tubercle. When lesions are extending there is frequently an overflow of monocytes into the blood-stream, with perhaps other cells of epithelioid character. On the other hand, when lymphocytes are in high concentration the prognosis has been found by long experience to be favorable. There appears to be a reciprocal relationship between monocytes and lymphocytes, the one being stimulated while the other is depressed. The monocyte-lymphocyte ratio in the peripheral blood has been found to reflect their relative proportions in the tissues and to form a basis for an index of the progress of the disease. Also, the original "native" M/L index in normal laboratory animals has been found to determine a predictable difference in susceptibility to the disease. In the evaluation of the differential count, Medlar has pointed out the significance attributable to the neutrophilic leucocytes in necrosis and cavitation. Altogether it would seem that the careful differential study of the blood cells may afford an additional instrument of precision in the analysis of clinical cases. Some clinicians now feel that it gives a more sensitive indication of what to expect in the individual case and how to proceed with exercise and other measures. *Chemico-Biological Studies in Coöperation with the National Tuberculosis Association Research Committee:* Of the biological studies thus far made, on a large scale, those with the lipoids have been carried furthest. The chemistry of the sugars and proteins, however, gives promise of results with important clinical application in the near future. At Yale University, Anderson and associates have partitioned the lipoids from human, avian, bovine, and the nonpathogenic acid-fast "timothy" organisms. The "phosphatide fraction," injected into the tissues, occasions a sterile reaction indistinguishable from that seen in tuberculosis. Epithelioid cells and Langhans' cells develop, with lymphocytic infiltrations, and regress without at any time causing embarrassment or clinical manifestations. Certain liquid, saturated fatty acids seem to carry the active principle and may elicit allergic phenomena in animals. On the other hand, the proteins and polysaccharides produce fever, haemorrhage, toxicity and sometimes death. When these various reactions are fully understood, the way will be cleared for the development of a purified protein for skin test use instead of the Old Tuberculin of varying composition and standard. When the phosphatide is given intravenously, in antigenic dosage, an antibody, apparently specific, is formed, as indicated by precipitin and complement-fixation tests and absorption experiments. When this is present in low titre an increase of epithelioid cells in the tissues may be found; conversely, when the serological reaction is more striking little cellular reaction is evident. *Implications of the Newer Bacteriological Studies:* The development by Petroff of a method for culturing acid-fast organisms on plates in single colonies has revolutionized our concepts, and for first time biological studies may be made with tubercle bacilli

on the same basis as in the more rapidly growing pyogenic group. It has been found that differences in virulence attend differences in colony development and morphology. The "S" colonies of avian and bovine tubercle bacilli are smooth, moist, moth-ball-like, easily emulsified, and made up of small pleomorphic faintly acid-fast organisms of marked virulence. The "R" colonies are rough, dry, granular, impossible to emulsify, and morphologically show typical clumps of long, beaded, strongly acid-fast, branching bacilli, of less virulence. Petroff's work brings out two points of clinical importance: *1:* It is essential that great care be exercised in staining sputum and other material so as not to overdecolorize and lose the small virulent organisms. Cooper's modification of the Ziehl-Neelsen stain, with the addition of 10 per cent sodium chloride to the carbol-fuchsin and counterstain of methyl-green, tends to fix and reveal in contrast all acid-fast organisms. *2:* An analysis of the percentage of different morphological forms is important. Petroff has followed individual cases through periods of spread with subsequent subsidence and found the percentage of "R" and "S" organisms to change in advance of the pathological developments. Doan has personally carried out some experiments with Petroff's methods and especially with the well-known avian strain, A1. Using both the R and S dissociates, he has observed in both chickens and rabbits the appearance of a few colonies of an opposite type to the original. Thus it seems that environmental conditions may modify essential characteristics and permit of mutations. For this reason there is danger inherent in any method of vaccination with living bacilli and no living virus should be used as a preventive or therapeutic measure. In perhaps no field of medicine at present are current concepts undergoing closer scrutiny, new experimental evidence accumulating more rapidly, or theories more in a state of flux than in tuberculosis. It behooves the clinician to be both alert and receptive, but also highly critical.—*The Relationship of Recent Investigations to Diagnosis and Prognosis in Clinical Tuberculosis*, C. *A. Doan, Meeting Massachusetts Med. Soc., June 17, 1930, reported in New England J. M., October 30, 1930, cciii. 862.*—(*A. P.*)

Pathology of Primary "Affect."—The author examined 350 cases postmortem between the ages of 11 months and 82 years, and in 101 of these there was a diagnosis of pulmonary tuberculosis. One hundred primary "Affects" of the lung and 115 primary complexes were examined. Of the latter there were 9 with caseous foci, 3 with chalky, 48 with calcified, 46 with bony and 8 with calcified bony foci. In one man 65 years of age there was found a late caseous primary "Affect." The foci were found 67 times in the right and 42 times in the left lung, and predominantly in the lower third of the upper lobe. Contrary to the observations of Küss lower-lobe foci were not found.—*Zur Kenntnis der Anatomie und Histologie des primären tuberkulösen Lungenaffektes, G. L. Derman, Virchow's Arch., 1930, cclxxv, 465.*—(*H. J. C.*)

Clinical Significance of Pathological Changes in Pulmonary Tuberculosis.—Ranke taught that there were four basic forms of pulmonary tuberculosis: (1) primary complex; (2) secondary stage; (3) tertiary stage, which is a continuation of (2) and showed localization in an organ with still individual haematogenous metastases; and (4) isolated phthisis. The author prefers a classification into two groups: a primitive phase with all the factors of the primary complex and finally ending in the haematogenous organic phthisis, the genuine isolated phthisis as an "alterative" phase. A differentiation of primary *Affekt* and reinfection appears untrue, since in the primary as well as in the "alterative" stage exogenous and endogenous superinfection and metastases can occur. The puberty phthisis of Aschoff is considered as a late primary complex. The roentgen procedure is valuable in determining the type of focal reaction. The anatomical diagnosis (exudative-destructive or productive-reparative) is significant, since it parallels the activity of the process. Anatomical data is, however, of little value alone and must be elaborated upon by the clinical findings.—*Die klinische Bedeutung pathomorphologischer Veränderungen bei der Lungentuberkulose, W. Bronkhorst, Beitr. z. Klin. d. Tuberk., 1930, lxxiii, 325.*—(*H. J. C.*)

Early Infiltration.—A case of early infiltrate is reported in a 19-year-old male with clinical and roentgenological and complete postmortem findings. There was found a solitary brain tubercle, probably part of a metastasis from "the reinfection" of the lung. The case verifies the existence of a nonapical early infiltration. The case consisted predominantly of exudative changes which are viewed as of a progressive nature. A primary focus in the lower lobe was also found with characteristic picture.—*Zur Morphologie und Genese des Frühinfiltrats, H. Kudlich and F. Reimann, Zeitschr. f. Tuberk., 1930, lv, 289.*—(*H. J. C.*)

Acute Tuberculosis without Apparent Localization.—The problem of acute forms

of tuberculosis gravitates around three important questions: *1: Clinical:* The study of the acute conditions ordinarily grouped a little vaguely under the head of bacillary septicaemia: miliary tuberculosis, bacillotuberculosis, subacute phthisis, typhobacillosis. Should one erect or remove their connections or barriers? Should they be classified among the clinical forms of pulmonary tuberculosis at all? Bard writes that tuberculous septicaemias should not be confused with ordinary tuberculous bacillaemias, and should be placed definitely outside the category of pulmonary tuberculosis, with which they are now provisionally associated under the hypothesis that they are really only discrete miliary forms or still latent parenchymal forms of that disease. *2: Pathological:* The rôle of the lymphatic system in the evolution of the tuberculous process. Leave to surgery cases of clear-cut localized adenitis. Eliminate also tracheobronchial adenopathy, such as described by Guéneau, Oelsnitz, d'Espine and Rist. Contrary to Parrot's law, according to which tuberculization of the mediastinal lymph nodes would be secondary to a primary pulmonary focus, Calmette has shown that infection of these nodes ("heart of the lymphatic system") might result from an intestinal, mesenteric or tonsillar portal of entry. Jousset, Bernard, Lelong and others have shown their importance as a point of departure for adult tuberculosis (reinfection). Sergent, in his studies of perilobulitis, has revealed the importance of the intrapulmonary lymphatics in its propagation and dissemination. Calmette, with Valtis, Boquet, Nègre, Arloing with Dufourt and Malartre, Sergent with Durand, Kourilsky and Benda, and finally Paisseau and coworkers, have shown that injection of the tuberculous "ultravirus" in guinea pigs provokes important lymphatic lesions and appears to have a special affinity for the lymphatic system. It localizes especially, according to Calmette, in the coronary, tracheobronchial and mediastinal lymph nodes. *3: Etiological:* What are the respective rôles of the bacillus and the "ultravirus?" Calmette distinguishes "bacillosis," which represents generally the terminal phase of an infection initiated by the ultravirus, and "pre-bacillary granulaemia," a more acute syndrome characterized by absence or rarity of normal acid-fast forms. Miliary tuberculosis ("granulie") represents a transitional phase or form in which both elements are present. *Case Report:* A girl of 18 was sent to Hauteville in April, 1929, by Casabianca, of Nice, for "bilateral cervical adenitis, presumably tuberculous, continued febrile state, wasting anaemia." A brother and two sisters had died of a "haemorrhagic fever." Her mother was healthy, her father suffered from cholelithiasis. She was born in Peru and came to France in 1923, where, although not quite as robust as before, she remained well up to January, 1928. At this time she had some haemoptyses and was said to have "involvement of the right apex," but this was not confirmed by X-ray and the clinical signs were doubtful. She spent ten months in Venice and all signs cleared up. In February, 1929, she had an eruption called measles lasting three days, with fever between 38° and 40°C., epistaxis and double cervical adenopathy. Laboratory, roentgenographic and clinical findings were negative except for a slight leucocytosis and polynucleosis. Nevertheless Casabianca considered her tuberculous. A consultant found a small ulceration of the nasal mucosa which he cauterized. There was no cough or expectoration. The patient was pale, wasted and asthenic, incapable of any effort. She ran fever between 38.5° and 39.5°C. and showed two elongated carotid chains of lymph nodes, 8 cm. in extent, 4 cm. broad, with no sign of fluctuation. There was no other adenopathy. The pulse was rapid, around 130, and blood-pressure low, 100 / 60. Liver and spleen were not felt. Over a period of two months the carotid nodes varied somewhat, increasing when the temperature fell and *vice versa.* Her general condition deteriorated. May 20, 1929, there appeared suddenly diffuse abdominal pains, predominating in the left iliac fossa, with vomiting and rapid thready pulse, then signs of obstruction. Michon, of Lyons, did an emergency laparotomy on the 21st and found an abundance of peritoneal fluid with disseminated tuberculous granulations of the ileum. Immediate closure was done. For two weeks she was a little better, less asthenic, and the lymph nodes decreased; then the temperature rose, the nodes increased, and asthenia returned. She became progressively cachectic and somnolent. July 1, 1929, for the first time, some polymorphous râles were heard over the pulmonary bases and she began to cough. On the 13th new abdominal signs appeared and she died. There was no necropsy. *Discussion:* Here we see an acute tuberculosis, the only constant localization being a carotid adenopathy. The process did try to settle on the ileum and there was a transitory eruptive phase. Reference to the case of a woman of 30, reported by Bernard, Salomon and Lelong, showed an intimate and prolonged contact with a tuberculous person, and later establishment of a "typhoidal febrile state" (a "typhobacillosis") lasting three weeks, subsiding by lysis. In this case roentgenography showed a persistent tracheobronchial adenopathy and

after three months' remission constitutional symptoms recurred, together with the development of an ulcerocaseous tuberculous peritonitis with abdominal lymph-node involvement, and finally a pulmonary tuberculosis, which lasted eight months, resulting in death. In what category should one place the case here recorded? According to Langeron, the clinical conception of the septicaemias is characterized by the notion of general phenomena predominating over local symptoms, and with the further desirable but not indispensable corollary of proof of an infectious agent in the blood-stream. In the case of tuberculosis such a condition is less well defined than in the ordinary septic infections. Langeron believes that true tuberculous septicaemia is very rare and difficult to demonstrate and that most often we are dealing with toxaemia from a deep-seated focus. To clarify the confusion in terms, Dumarest and Mollard describe three categories of acute tuberculosis without apparent localization: miliary disease ("granulie"), acute bacillotuberculosis (Landouzy's subacute phthisis) and typhobacillosis (Landouzy). *1: Acute Miliary Tuberculosis (Granulitis)*: Until a few years ago, wrote Bezançon and Delarue, few conceptions seemed to rest on a more solid basis, but now the classical conception no longer holds. We are no longer dealing with a fixed acute type of tuberculosis which is entirely distinct from caseous pneumonia or chronic phthisis. In the first place, the dogma of exclusively follicular structure has been found unsound, because an exudative alveolitis or even fibrous elements may complicate the picture at various stages. Bezançon and Delarue think that it might be better to employ the term "disseminated nodules," which implies nothing as to their histological structure. In the second place, the dogma of dramatic clinical evolution, typhoid or asphyxic, according to whether the granules are generalized or predominate in the lung, does not keep its original rigidity. Disseminated granulations may or may not be the substratum of the only fatal type (that of Empis). They may also develop slowly or even heal. In 1901 Bard drew attention to local, subacute forms, which he found more frequent than the classical acute type, and which often recovered. This observation has been abundantly confirmed, and such terms as "torpid occult miliary disease of childhood" (Nobécourt), "migratory" or "cold" granulitis (Burnand and Sayé, Rist, Rolland, Jacob and Hautefeuille). Thus, deprived of both its anatomical and clinical criteria, miliary tuberculosis no longer stands out as an entity, except in the following respect: the diffusion of the infectious agent through the blood-stream is its precursor. In this respect it is distinct from the massive bronchopneumonic lesions of caseous pneumonia, which are manifestly due to endobronchial implantation. *2. Subacute Phthisis:* Bernard has well described the subacute septicaemic type of Landouzy and Laederich. This form simulates the septicaemias caused by ordinary microörganisms. Certain clinical features suggest tuberculosis, such as multiple nodular erythema, with fever. Certain larval forms get well, but more are fatal. Necropsy shows few or no follicular lesions. This group resembles "primary intravenous syphilitic infection." No chancre in the latter case. No point of primary localization in the former. *3: Typhobacillosis:* This Landouzy considered as a primary, essential septicaemia, which however tended eventually to fixation in the lung, or serous membranes (meninges, pleura, peritoneum). The hypothesis of no primary localization, however, was criticized by Hutinel in 1911 and more recently by Ravina and others. Some assume a discrete pulmonary focus, or a lymphatic one, as the cause of the general symptoms. Dumarest and Mollard believe "typhobacillosis" is caused by lesions but that these are distinct from miliary disease. In their case reported the carotid lymph nodes were involved, in Bernard's the hilar nodes. One may find an analogy in typhoid fever, in which Eberth's bacillus sets up an allergic inflammatory state of Peyer's patches in the submucosa of the terminal part of the small intestine. Hutinel, in 1908, observed the frequent association of adenopathies and typhobacillosis and remarked that tuberculous mediastinal adenopathy, considered clinically cured, might be reactivated and become the point of departure for a generalized tuberculosis of grave prognosis. In a series of children dying of tuberculous meningitis he found the mediastinal lymph nodes always tuberculous, and caseous in one-half the cases. He states that he could multiply examples of typhobacillosis in which appeared, first, signs of tracheobronchial adenopathy, then pulmonary, pleural and peritoneal developments, and that inflammatory, nodular or degenerative reactions in these lymph nodes may suffice to explain the fever and constitutional symptoms of so called "typhobacillosis." There is again the explanation of fever from poisons formed in the caseous foci, and Hutinel believes true tuberculous septicaemias are rare. It is especially in the writings of Bernard, Salomon and Lelong that the idea of a lymphatic origin of "typhobacillosis" is met with, and they argue that this manifestation of acute nonpulmonary tuberculosis is fundamentally a lymphatic one. *Conclusions:* There are

three possible types of acute nonpulmonary tuberculosis: (1) subacute septicaemic phthisis, without localization, and of doubtful entity, (2) miliary tuberculosis, or granulitis, with variable lesions, blood-borne, and (3) typhobacillosis, or acute tuberculosis of the lymphatic system. Clinically these can scarcely be differentiated. Any patient with prolonged fever should be most carefully studied, first in order to eliminate nontuberculous infections. Roentgenographs of the chest may show a deep-seated adenopathy or a discrete miliary development. Only when every attempt at localization is negative should one speak of "typhobacillosis" or "intravenous" (septicaemic) tuberculosis. Certain interhilar adenopathies may be missed, even with roentgenographic aid, and none of the classical signs may be present. The question of where the primary infection began will arise and cannot always be settled. In the case reported it is not clear.—*Les tuberculoses aigues sans localisation apparente, F. Dumarest and H. Mollard, Rev. d. l. Tuberc., July, 1930, xi, 735.*—(*A. P.*)

Pathology of Miliary Pulmonary Tubercles.—Quite recently there has been a lively controversy concerning "granulitis" (miliary tuberculosis), especially as to its anatomical substratum and mode of formation of the miliary nodules. The present discussion is based on 42 cases observed at the clinic of the *Hôpital Saint-Antoine*, together with pathological studies made in Roussy's laboratory. What exactly are these little rounded bodies, disseminated in the pulmonary parenchyma, as well as in other organs, that Bayle and later Laennec described as "granulations?" Virchow regarded them as produced by "cellular proliferation," which resulted in "gray tuberculous neoplasia" or "gray granulation." Luys, Robin, Empis considered them so different from ordinary tubercle as to warrant a specific name, *la granulie*, characterized by an eruption of "fibroplastic" granulations. Once this error was recognized, the terminology of Empis, from a pathological view-point, still seemed based on immutable characteristics: the expression of haematogenous bacillary dissemination, with an anatomical substratum of granulations formed by an agglomeration of follicles of the epithelioid giant-cell type, located in the vicinity of vessels or capillaries and built up on a connective-tissue basis, not involving the alveoli, hence "interstitial." Such a conception was made to fit not only the "generalized" but the "pulmonary" forms of the disease,—asphyxic, catarrhal, etc. Despite objections by Tripier, Rénon and Géraudel, the "interstitial follicular nodule" was considered the fundamental lesion. In 1922 Bezançon, Letulle and Braun reported 3 observations of "acute asphyxic tuberculosis" in which the nodular formations had no such structure but were made up of islands of caseous alveolitis. This was the beginning of the dismemberment of the old clinicopathological conceptions and the construction of another of dual scheme, including both haematogenous granulations and bronchogenic miliary tubercles. This, however, led to confusion among French as well as other authors. In Germany Aschoff and Huebschmann, in Austria Korteweg and Loeffler, constructed still other and different schemes and classifications. In France the most important work of this order has been that of Rist, Rolland, Jacob and Hautefeuille. The latter have observed that even in the case of *granulies généralisées*, the lesions may be nonfollicular and alveolar. While Virchow's description of the "gray granulation" is undoubtedly the most frequent lesion in the viscera (liver, spleen, kidneys) in cases of generalized granulitis, in the lungs, especially where the pulmonary lesions are numerous, they are much more diverse. In certain cases there are islands of alveolitis with no follicular elements, "exudative nodules," following the classification of Aschoff-Nicol. In other cases all the nodules are made up of epithelioid giant-cell agglomerations, with central caseation. These nodules, as shown on section, are nearly always periacinous, and show near their centre elastic fibres, vestiges of destroyed alveolar walls. In other cases the collagenous element predominates. There are also mixed exudative and follicular nodules. In still others, although there is no typical follicular structure, there is a connective-tissue basis. Can the histological structure be determined from the macroscopic appearance? Rénon and Géraudel have shown that there is no invariable correspondence, as have Rist, Rolland, Jacob and Hautefeuille. It therefore seems that "miliary granulations" and "miliary tubercles" cannot be differentiated and it would be preferable to supplant them by the more inclusive term "miliary nodules." Another question: can one determine from the topography of the nodules the path of infection? Miliary nodules, as already observed, may vary in topography. They may be uniformly disseminated, homogeneous, and situated especially about the blood-vessels. This is the classical picture as described by Letulle. On the other hand, they may present special groupings, in the form of corymbs or rosettes; here the microscope shows confluent nodules, often about a bronchiole. However, if peribronchial nodules appear to be sometimes of aerial origin, they may also be of haematoge-

nous origin; likewise, the perivascular situation of the lesions does not necessarily imply that the bacilli were blood-borne. It seems that the common site of the lesions in the adventitial layer points toward a tuberculous lymphangitis. It has been shown that bacilli brought by the blood do not create only interstitial lesions. Aschoff, Seemann, and others, have shown that from the capillaries there occurs a veritable "excretion" of bacilli into the alveoli, setting up an exudative alveolitis, and that follicular nodules usually present also an acinous topography. *Clinico-pathological Groups of Lesions:* As shown above, there exists no precise anatomical substratum for "typhoidal," "suffocating" or "catarrhal" types. On the two latter, however, exudative nodules surrounded by diffuse parenchymal splenization are most common. In the rapidly fatal forms one finds at necropsy only exudative lesions; in the more prolonged forms fibrous and follicular nodules occur. The so called "asphyctic" forms are associated with nodules of exudative alveolitis. So called "cold granulitis" (*granulie froide*) is characterized by fibrous nodules, corresponding to Bayle's "miliary granulations." Between these two extremes come the less acute and subacute forms with mixed lesions. On this basis one may speak of (1) exudative nodules, (2) intermediary nodules, (3) follicular nodules and (4) fibrous nodules, not as totally different lesions but as different stages of evolution of one and the same process. What characterizes "granulitis" and makes it an entity is the dissemination of the lesions. Such a dissemination seems to be the expression of a haematogenous mode of entry. Should the generic term of *granulie* be abandoned, as advocated by Rist, Rolland, Jacob and Hautefeuille? There seems to be no need for this if it is kept in mind as synonymous with the foreign term "miliary tuberculosis," as its usage is well established.—*Remarques sur la structure et le mode de formation des nodules miliaires des poumons, F. Bezançon and J. Delarue, Section d'études scientifiques de l'Oeuvre de la Tuberculose, May 12, 1930, reported in Rev. d. l Tuberc., July, 1930, xi, 808.*—(*A. P.*)

Tuberculosis with Multiple Localizations.—During the early months of life the patient developed a suppurative cervical adenitis. At 8 years of age, an osteoarticular tuberculosis became manifest in the right tibiotarsal joint, right elbow, metacarpophalangeal joint of the left thumb and phalanx of the little finger. These lesions were curretted many times. When the patient was twelve years old the aforementioned lesions became fistulous and healing was complete after three years. At 14, a left coxalgia with abscess and fistula-formation was diagnosed. Healing occurred without ankylosis. Between the ages of 24 and 27 the patient was bedridden with a fibrocaseous peritonitis which necessitated seven operations for the evacuation of abscesses and a later laparotomy for intestinal obstruction. At 27 years, a left tuberculous kidney was removed. Two years later the dormant bone and joint lesions became reactivated and a cold abscess developed in the left elbow. Then the peritoneal lesions flared up again. Following a long period of fever and cachexia, the patient began a very gradual improvement. During the past ten years she has enjoyed good health and has worked uninterruptedly. The diagnoses of tuberculosis were confirmed by laboratory tests.—*Tuberculose grave a localisations multiples: osseuses, articulaires, ganglionaires, péritonéales, renales. Guérison Complète depuis dix ans, Michaux and Albot, Meeting Soc. Méd. des Hop., November 8, 1929, reported in Progrès Méd, November 23, 1929, no. 48, 1929.*—(*U. E. Z.*)

Chronic Forms of Disseminated Tuberculosis.—The author reports on several cases of abortive haematogenous forms of pulmonary tuberculosis. The roentgen pictures are explained on the basis of the entrance of a virus into the lymph channels of alveolar septa. The induration of the lesions may cause disturbance in the pulmonary circulation, leading to decompensation. Tuberculin hypersensitiveness in these forms is slight or may be entirely absent.—*Über torpide Formen disseminierter Tuberkulose, L. Hantschmann, Beitr. z. Klin. d. Tuberk., 1930, lxxiii, 688.*—(*H. J. C.*)

Fatty Infiltration of Pulmonary Veins.—While regressive changes in most blood-vessels have been studied thoroughly there are no systematic studies of pulmonary veins on record. A total of 60 cases was examined; some degree of fatty changes was found in 38 of these. The fatty infiltration may be localized in the elastic tissue or outside of it. In cases of isolated fatty infiltration of the inner elastic lamella, minute fat droplets are seen along the course of the elastic membrane, while the elastic fibres are separated into small granules. In more marked cases, the elastic lamella is split and broadened, and, at times, hyalinized in parts. In other cases a diffuse infiltration of all elastic elements is observed. The intima shows fatty deposits both intracellularly and extracellularly; massive infiltrations with lime deposits are rare. At the boundary between intima and media, the fatty deposits have been identified as a

mixture of cholesterol and fatty acids; the deposits within the elastic elements are fatty acids and soaps; and the small isolated droplets are cholesterol, glycerolesters and cholesterolesters. The fatty infiltration of pulmonary veins does not show a definite relation to atheromatous changes in arteries nor to such intra- or extrapulmonary processes that increase the blood-pressure in the pulmonary circulation.—*Ueber Verfettung der Lungenvenen, R. Prêvôt, Centralbl. f. allg. Path. u. path. Anat., January 20, 1931, i, 305.*—(*M. P.*)

Tuberculous Cavities.—Certain soft shadows in the roentgenogram in pulmonary tuberculosis are considered as precavernous demarcations without disintegration. This is understood to be a ringing of a section of tissue by means of cellular infiltration without central destruction. In such a focus all cavity symptoms must be lacking, including tubercle bacilli and elastic fibres. The rapid disappearance of large ring shadows in the roentgenogram, especially to complete disappearance, is viewed as being a shallow cavity in which the closely approximating walls become adherent either as the result of or without collapse therapy.—*Zum Problem der tuberkulösen Kaverne. I. Einiges Grundsätzliche zur Frage der Entstehung, Erkennung und Heilung tuberkulöser Kavernen, H. Alexander, Zeitschr. f. Tuberk., 1930, lxi, 1.*—(*H. J. C.*)

Healing of Cavities.—Four interesting cases, three of them in the secondary stage, resulted in spontaneous healing of cavities. It is, however, concluded that the spontaneous healing of cavities cannot be depended upon and that pneumothorax should be utilized after a certain period of observation.—*Kasuistischer Beitrag zur Frage der Kavernenheilung, H. U. Ritschel, Zeitschr. f. Tuberk., 1930, lxi, 121.*—(*H. J. C.*)

Healing of Tuberculosis.—Healing in tuberculosis in the immune or adult type is accomplished through several different processes: (1) destruction of bacilli; (2) retardation of the passage of bacilli through the tissues; (3) elimination of bacilli through natural channels by caseation and cavity-formation; (4) development of a state of desensitization to bacillary and other toxins; (5) encapsulation of, or rendering inactive, viable bacilli which remain in the tissues; (6) ridding the body of the inflammatory products which accompany the infection; and (7) repair of the injury inflicted upon the body by the disease. One gets the impression that healing depends upon controlling the size and the effects of the reinoculations and keeping them within the range of the individual powers to cope with them. To this end the acquired bactericidal action of immune tissues, the retarding influence of the allergic inflammation upon the passage of bacilli through the tissues, and the desensitization of the host of toxic substances, are probably the major contributing factors. Therapy is aimed at creating the best possible physiological balance, and at keeping the infection quantitatively and qualitatively as mild as possible. Rest is a matter of necessity, as exercise during active disease favors extension of infection, increase of toxaemia, and lowering of resistance. Rest to the lung itself by shot-bag compression, operations on the phrenic nerve, pneumothorax, or thoracoplasty is of further value. Well-balanced diets, containing adequate calories, vitamines and salts, are necessary to the best progress against the disease. In the final analysis the patient is healed by his own immunity mechanism. The effects of the patient's own reinoculations of bacilli or bacillary protein are helpful in promoting healing unless too severe. If very severe, they may be harmful, but the necessary immunity to heal cannot be secured without them.—*Healing of Tuberculosis, F. M. Pottenger, Ann. Int. Med., September, 1930, iv, 281.*—(*R. D.*)

Cells Found in Tuberculous Tissues.—The aetiology of the epithelioid cell and its relationship to the other mononuclear cells in tuberculous tissues, and to the normal connective-tissue cells, are largely questions of conjecture. Cunningham, Sabin, *et al.* consider that the epithelioid cell is derived from the monocyte. Most of the workers with vital dyes consider that the epithelioid cell, as defined in the less specific and more general sense of the large mononuclear cell of tuberculous tissues, arises from the large phagocytic cell of the connective tissues. In the present study the methods of fixed, vital and supravital staining were combined in order to determine the relationship between the vitally stained cells in the tissues and those which stain supravitally with neutral-red. The experiments may be separated into two groups. These represent respectively studies of chronic tuberculosis in animals given trypan-blue after the infection had been present some time, and studies of early tuberculosis in animals, which had been vitally stained previous to inoculation. At the time of autopsy, supravital studies were made of scrapings from the lungs, livers, spleens, lymph nodes and at times of peritoneal exudates and omental spreads. Tissues from the same organs were fixed and sectioned. The results show that the mass of the large mononuclear cells composing

the tuberculous area consist of a number of varieties. There were monocytes, clasmatocytes and epithelioid cells, as well as many degenerating cells of these three types, and giant cells, which by their manner of storing the two dyes, gave evidence of having developed from the various types of mononuclear cells. The monocytes rarely contained the vital dye, while the clasmatocytes stored great quantities of it. The epithelioid cells were found both with and without the vital dye. Transitions could be traced, not only between the monocyte and the epithelioid cells, but also between the clasmatocytes and the epithelioid cell. The monocytes and clasmatocytes were present in numbers in excess of the normal. Under the influence of the infection, each exhibited changes which resulted in modified forms which more and more departed from the original cellular types and partook of the characteristics of the same final type, that of the epithelioid cell. Both the monocytes and the clasmatocytes were frequently seen to contain bacilli. It seems very likely that the organisms were, therefore, the causative factor of the changes, and worked from within the cells to produce modifications of such a nature that both types of cells assumed similar characteristics, and became the typical epithelioid cells found in tuberculous tissues. Both of these cells were actively phagocytic in their normal state, the clasmatocyte being more so than the monocyte. *Summary:* The large mononuclear cells found in the tuberculous areas consisted of monocytes, clasmatocytes and epithelioid cells, together with transitional and degenerate forms of the same cells. By means of the superimposition of the supravital upon the vital dye, transitions could be followed from clasmatocytes to epithelioid cells, as well as from monocytes to epithelioid cells. The types of staining observed in giant cells were analogous to those observed in the mononuclear cells. The concept has been developed that, in tuberculosis, some toxic factor, acting either from within or from without the cells, affects the functions of both the monocytes and clasmatocytes, so that these cells become modified both in morphology and in activity, and develop into characteristic epithelioid cells, or into giant cells, or die and degenerate at any stage in the course of these changes.—*The Cells Found in Tuberculous Tissues as Demonstrated by Vital and Supravital Staining. E. H. Tompkins and R. S. Cunningham, Bull. Johns Hopkins Hosp., January, 1931, xlviii, 8.*—*(F. G. P.)*

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